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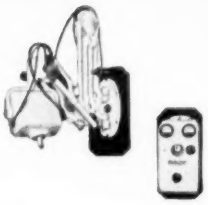

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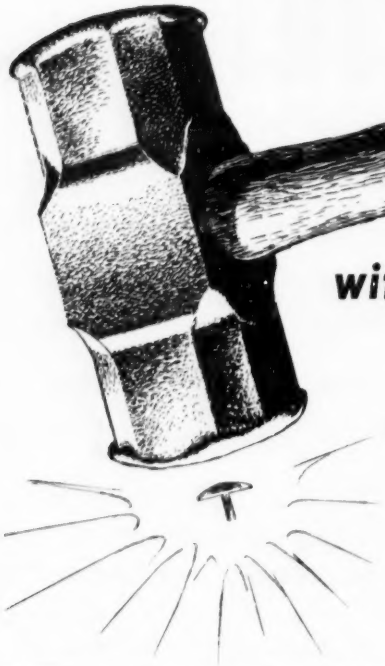

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1. Sayer, R. J., et al.: Am. J. M. Sc. 221:256 (Mar.) 1951.
2. Welch, H.: Ann. New York Acad. Sc. 53:253 (Sept.) 1950.
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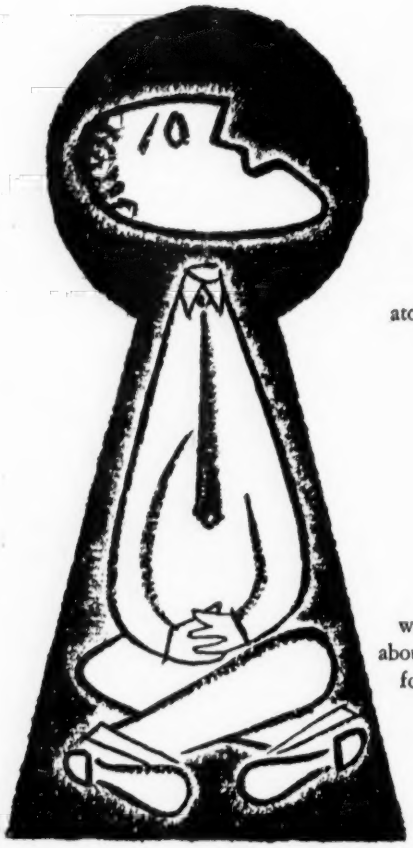

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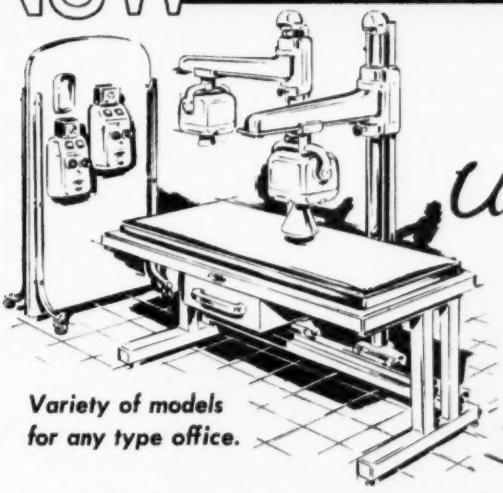

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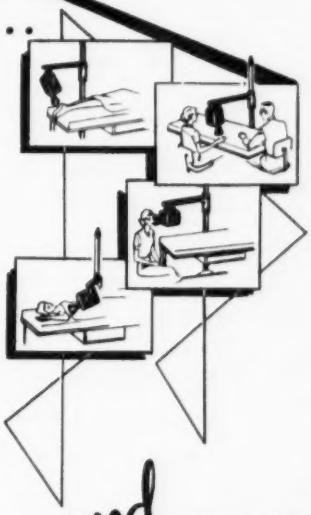

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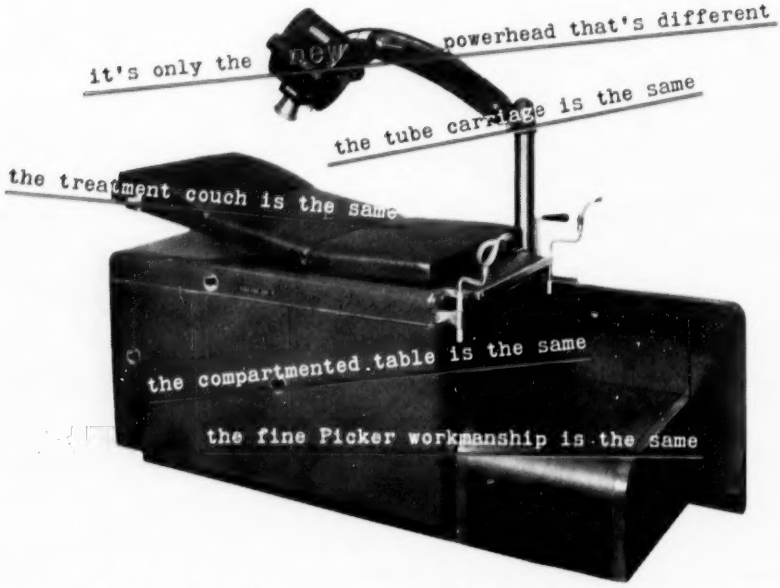
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Editorial

EXPERIMENTAL ANIMAL RESEARCH

The report by Callaway and Hambrick in this issue represents an enormous and arduous task which will serve a useful purpose if it does no more than to spotlight a troublesome situation that confronts the entire medical profession too often—that is, the shameful need to defend repeatedly against the misguided but frequently effective efforts of antivivisectionists to abolish animal experimentation.

The benefits to mankind from animal experimentation have been recited time and again, but even in dermatology, where because of structural and biological differences animal skins are not always ideal for study, the rewards have been significant—in studies of permeability and absorptive powers of the skin so important to the therapist and the commercial chemist, in studies of anaphylaxis and sensitization, in the study of infections of all sorts, particularly tuberculosis, in pigmentation, tumor formation, metabolism, nutrition, in fact in almost every phase of dermatology. The benefits though enormous, are yet insignificant as compared to the value of animal experimentation in other fields of medicine, in pharmacology and in surgery in particular. The knowledge gained is of course ultimately passed on to mankind so that even those poor souls who support antivivisectionism profit by it.

They are an organized and apparently well financed group who constantly exert tremendous influence upon unenlightened legislators. Medicine and mankind would suffere immeasurably were they to succeed.

NODULAR GRANULOMATOUS PERIFOLLICULITIS OF THE LEGS CAUSED BY TRICHOPHYTON RUBRUM

J. WALTER WILSON, M.D.
ORDA A. PLUNKETT, Ph.D.
AND
AVIS GREGERSEN, F.B.P.A.
LOS ANGELES

THE FUNGI in the group known as the "dermatophytes" acquired the name because of their propensity for limiting their pathogenic activities to the skin; their inability to survive in any of the deeper tissues of the body usually has been accepted as well established. In fact, in all but a small percentage of instances their range is even narrower, so that terms such as "epidermatophytes" or "keratophytes" might have been considered equally appropriate; they luxuriate in the keratin portions of the epidermis, the hair and the nails; they thrive less well in the rete and do not ordinarily penetrate deeper than the basal cell layer.

There are, however, at least three exceptions to this rule, two of which are well recognized and commonly encountered, constituting the clinical entities known as kerion Celsi and its variants and the polymorphic allergic manifestations classified as "dermatophytids." The third is but poorly understood, infrequently reported, and usually referred to as the "trichophytic granuloma of Majocchi."

The present study was stimulated by the discovery that in California an entity resembling Majocchi's trichophytic granuloma in many respects is not uncommon. It is not a new disease, having apparently been present for at least a decade without its fungous nature being previously recognized. It offers an opportunity for accurate dermatologic and mycologic diagnosis to provide a cure for an otherwise chronic, persisting, scarring disorder. From the observation of 14 cases certain tentative conclusions have been drawn, which seem to clarify the subject sufficiently to warrant publication.

REPORT OF CASES

CASE 1.—As has been previously reported,[1] a 54-year-old white woman sustained a bruise just above the left ankle on the medial surface. After the acute phase of this injury had subsided, an eczematous eruption was noted near the periphery, which persisted and enlarged during the ensuing year, in spite of a variety of medicaments and x-ray therapy, until an area 5 by 8 cm. had become involved. The borders of the plaque were not sharply delineated; the color was dusky red, and there was considerable scaling. Two unusual features were noted, consisting of several deep-seated firm slightly tender nodules ranging up to 7 mm. in diameter

Read before the meeting of the American Dermatological Association, Lake Placid, N. Y., June 10, 1953.

From the University of Southern California, Department of Medicine (Dermatology and Syphilology) M. E. Obermayer, M.D., Chairman (Dr. Wilson and Miss Gregersen) and the University of California at Los Angeles, Department of Botany (Dr. Plunkett).

and adherent to the skin, scattered discretely throughout the area, and a few atrophic discoid scars of similar size. The clinical diagnosis was doubtful, but tuberculosis indurativa, stasic dermatitis with localzed thrombophlebitis, nodular vasculitis, and an infectious granulomatous process were considered. The presence of the nodules and scars seemed to rule out a dermatophytosis with sufficient certainty so that direct microscopic examination of wet preparations of epidermis was not done at that time.

A specimen was removed from the center of one of the nodules for biopsy. Fragments were cut from one side of the deeper portion and inoculated into aerobic and anerobic bacteriologic media as well as onto Sabouraud's glucose agar. Trichophyton rubrum was the only organism recovered; it arose from each of three inoculations on Sabouraud's medium.

In the histopathologic preparations stained by hematoxylin and eosin fungus elements were not seen on first examination, but staining by the Hotchkiss-McManus method revealed an oval lobule about 40 μ in diameter situated deep in the corium and consisting entirely of rounded spores about 2 μ in diameter, some in chains, suggesting arthrospore formation. No hair elements were found in association, and no evidence of the remains of a follicular wall could be discovered anywhere in the vicinity. The fungus cells took the stain well; they appeared to be healthy and were not in the least disintegrated. (That they yielded cultures proved their viability.) Surrounding this lobule was a chronic granulomatous infiltrate, which will be described in detail later.

Subsequently, T. rubrum was demonstrated by direct examination and culture in material taken from the superficial scales at the edge of the plaque of dermatitis, as well as from several toe nails. It was thus apparent that the fungous nature of the disease could have been ascertained earlier and by simpler means had not the nodules misdirected the clinician's attention toward other entities.

The intracutaneous injection of trichophytin produced no reaction, even when undiluted material was used. A blood cell count was normal, as was the fasting blood-sugar level.

The therapy employed in this case and in those which follow will be discussed later.

Case 2.—One of the dermatologists* who witnessed the presentation of Case 1 before the Los Angeles Dermatological Society, in February, 1951, saw in this case a close resemblance to the eruption exhibited by a patient who had recently come under her care. A 27-year-old dark-brown-haired and brown-eyed white woman had had a plaque of dermatitis for about one year, involving the entire calf of one leg and extending almost to the ankle. Nodules of all sizes up to 8 mm. in diameter were palpable throughout the area, some discrete and some in groups. There was no ulceration or pustulation, but several small circular scars were visible. The previous diagnosis had been erythema induratum of mild degree. When a specimen was removed for biopsy and cultures were inoculated with material obtained from the deeper surfaces of the specimen, T. rubrum was obtained. Histopathologic preparations stained with the Hotchkiss-McManus method revealed rounded bodies, some of which were identical in size and staining characteristics with those seen in Case 1, although not in such a concentrated mass. In addition, however, some of these spherules were much larger than was to be expected from any previous experience with any species of Trichophyton, ranging up to 6 μ in diameter. All gradations in size were observed, however, making it rather difficult to believe that they could be anything else but elements of T. rubrum (Fig. *D*). The same chronic granulomatous reaction was observed as in Case 1.

Case 3.—A 28-year-old dark-haired white woman had had about twenty "boils which never came to a head" on the posterior surface of her left leg during the preceding four years. Three or four had been present simultaneously on most occasions; each lesion had persisted for at least four months, and several had already subsided spontaneously, some with and some without leaving small circular atrophic scars. The patient had noted that in the early phase each nodule appeared to have hair in its center, which showed no tendency to fall from the follicle. Extraction of such a hair had not noticeably hastened the healing of the nodule surrounding it. Biopsy of a nodule revealed the same picture as in Case 2, and T. rubrum was recovered from material taken from the under surface of the specimen.

* Dr. F. L. Kettenbach.

During the succeeding two years 10 additional patients who presented a similar clinical picture were discovered by dermatologists in California.† To conserve space, those features which were displayed by all will be recorded here and only the important variations will be discussed later.

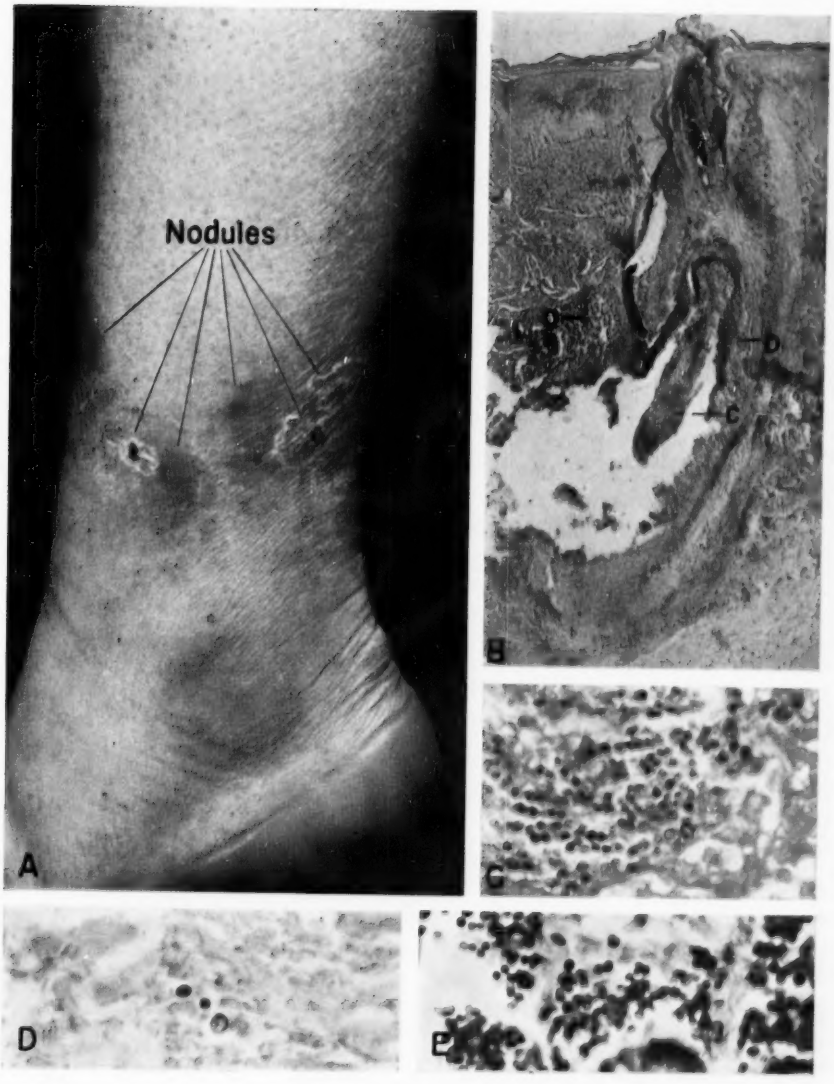
Cases 4 to 13, inclusive.—All patients have been dark-haired women from 19 to 50 years of age. The disorder has been limited to that portion of the legs between the ankles and two-thirds of the distance to the knees, principally on the posterior, lateral, and medial surfaces. The duration has been from three months to eight years. In all but two cases the disease has remained unilateral throughout its course. An area, usually consisting of a single plaque, of chronic dermatitis, varying from 3 to 20 cm. in diameter and irregular in outline, has always been present. A slightly cyanotic erythema is characteristic. Scaling in a variable amount has been a consistent feature. Firmly indurated nodules (Fig., *A*) have been present in variable numbers from a few to 20, never more than slightly raised above the surrounding surface, and more often not at all, being situated entirely below the flat cutaneous level. These nodules have been only slightly tender on pressure and not spontaneously painful; in most instances pruritus has been mild or absent. Individual nodules have persisted with little change for three or four months, after which spontaneous regression has occurred, somewhat less than half of them leaving small slightly depressed circular atrophic scars. Pustulation has not been observed, but necrosis with ulceration and crust formation has occurred in the later stages of the development of many nodules, followed by slow healing by granulation, requiring several weeks.

Intracutaneous testing with trichophyton was carried out in all but three cases; there were no strongly positive reactions, four were mildly positive, and seven were negative.

T. rubrum has been recovered in culture in all instances; no other fungus has been encountered in patients exhibiting this syndrome. The material for inoculation was obtained from the deeper surfaces of a specimen removed for biopsy, with the exception of two instances in which biopsy was not permitted.

Histopathologic preparations, when serially sectioned and stained with the Hotchkiss-McManus method, have usually revealed follicles which contained hairs in association with which fungous spores were usually present in profusion; an ectothrix mosaic arrangement of roughly spherical spores about 2 μ in diameter was typical (Fig., *Bb*), but, in addition, chains of such spores together with short hyphal segments were seen to be situated within the hair shafts (endothrix) (Fig., *Bc*). A varying degree of distortion of the deeper portions of the follicle has been observed; at certain points there were breaks in the continuity of all layers of the follicular wall, from which large areas of granulomatous infiltrate were seen extending laterally into the corium (Fig., *Ba*). This infiltrate was composed predominantly of epithelioid cells in a matrix of necrobiotic elements derived from the corium. Except for occasional tiny foci, there was nothing to suggest an acute inflammatory process, as is usually encountered in a pustule or abscess, or an allergic mechanism, as seen in a papule of a dermatophytid. Globular structures, sometimes in chains (Fig., *C*), sometimes in mosaic masses (Fig., *E*), and recognizable beyond doubt as being of fungous origin by comparison with the cells seen in and about the hairs, were discovered in these granulomatous areas; in some cases these elements have been very few, in others large oval masses composed entirely of such cells have been seen. Wherever the fungus cells were few in number, a surprising variation in their size was observed, some being 6 μ in diameter (Fig., *D*). At first it was difficult to accept these large globoid cells as being derived from T. rubrum, since none of such size has been previously reported to arise from any dermatophyte. However, it was easy to follow all gradations in size and staining characteristics downward to those which were indubitably of this nature. The selectivity of the Hotchkiss-McManus stain also made this interpretation unavoidable. A careful search through the granulomatous areas failed to reveal any hair fragments, cortical cells, or follicular keratin elements which might

† Cases were contributed to this study by Drs. Walter R. Nickel, San Diego; Max E. Krause, Oakland; Leonard C. Greenfield, San Diego; Lawrence Nelson, Santa Barbara; Walter F. Schwartz, Pasadena, and Philip K. Allen and Roberts B. Pappenfort, San Diego. One of the authors (J. W. W.) examined several of these patients clinically, and all cultures and histopathologic preparations were presented to both of us for study.



Clinical and histopathological features of nodular granulomatous perifolliculitis of the legs caused by Trichophyton rubrum. *A*, clinical appearance of the syndrome. *B*, *C*, *D*, and *E*, histopathologic preparations stained by the Hotchkiss-McManus method. *B*, vertical section through perifollicular granulomatous nodule; × 100; *a*, granulomatous infiltrate containing scattered fungus elements; *b*, ectothrix mantle of globular fungus spores; *c*, endothrix involvement showing chains of rounded spores and short hyphal fragments. *C*, spores in chains in granulomatous infiltrate; × 440. *D*, variations in size of spores; × 440. *E*, globular spores in mosaic masses in granulomatous infiltrate; × 440.

support the fungus in its usual parasitic role; the appearance of the fungal elements, however, strongly suggested that they were healthy, even when so far removed from their usual source of nutrition.

CASE 14.—Midway in this study Dr. Nelson Paul Anderson, of Los Angeles, presented to us two photographs in color depicting a syndrome apparently identical to that under discussion. These had been taken in March, 1941, and were labeled at that time "Dermatophytosis Caused by T. Purpureum, with Erythema-Nodosum-Like Leg Lesions." In spite of the fact that the patient did not permit further diagnostic procedures or treatment, we share Dr. Anderson's conviction that the case belongs in this group.

DIFFERENTIAL DIAGNOSIS

DIFFENTIATION FROM OTHER MYCOTIC DISORDERS

A. *Relationship to Kerion.*—It is apparent that the syndrome delineated above differs extensively from the reaction known as kerion Celsi, which occurs so frequently in the course of tinea capitis and in which two mechanisms are usually clearly involved.

The first is the sudden development and concurrence in the host of an allergic hypersensitivity to the fungus or its products, a process which indeed probably initiates the kerion reaction by causing local tumefaction, erythema, exudation, and epilation in the areas most severely involved in the infection. Frequently this reaction is accompanied by the appearance in other parts of the body of dermatophytids, indicating hematogenous dissemination of toxic materials of mycotic origin from the original foci, acting in conjunction with the hypersensitivity. In keeping with this concept, such patients are usually highly reactive to intracutaneously injected trichophytin. Although the term "kerion" is most frequently applied to this process when the scalp is the area involved, its identical counterpart occurs on the bearded skin in tinea barbae. Also closely simulating kerion is the process known as "tinea profunda," which may occur on any part of the glabrous skin, especially when the infection has resulted from contact with cattle or rabbits, and is caused by T. faviforme or T. mentagrophytes.‡ In some manner not yet clarified, and perhaps not even pertinently involved, this allergic hypersensitivity is usually associated with the development of a significant degree of specific immunity acting against the infection. As a consequence, spontaneous healing usually follows the appearance of kerion or its equivalent, and the entire infectious process is automatically limited to an acute or subacute course.

The second mechanism usually involved in kerion formation is that of the development of secondary infection with pyogenic bacteria, which results in pustulation, abscess formation, confluence of contiguous lesions, and necrotic destruction of tissue of such degree as to lead eventually to scar formation involving areas several centimeters in diameter.

In contrast, the disease under consideration is not associated in any demonstrable manner with the development of specific hypersensitivity; the local inflammatory reaction is characterized by an absence of acute features attributable to it, such as vesiculation and exudation, and in no instance in this series has a dermatophytid been encountered. Furthermore, the entire syndrome apparently bears no relationship whatever to the trichophytin reaction, the percentage of these patients reacting positively to this test being not significantly greater than that to be expected in the

‡ References 2-5.

urban population at large. In view of this absence of demonstrable hypersensitivity, it is not surprising to note that the development of immunologic resistance which usually accompanies that reaction seems also to be entirely absent. Consequently the disorder shows no tendency toward spontaneous regression but follows an exceedingly chronic, torpid course, wherein individual nodules may endure for months and the entire infectious process for years. There is usually no pustulation or abscess formation; in fact, secondary bacterial infection in even slight degrees has been noted but rarely. It is true that some lesions do become necrotic, and these, together with others to a total of perhaps one-half of the original nodules, eventually cause scarring; these scars are usually less than a centimeter in diameter and are discrete, while in kerion the individual lesions coalesce and form large scars.

B. *Relationship to Dermatophytid.*—The preceding paragraphs also contain the facts on which is based the conclusion that this type of nodular granulomatous perifolliculitis cannot possibly be considered to be a dermatophytid of yet a different sort than that seen in association with a kerion reaction. If it were, the onset should be sudden; the inflammatory elements should be of the acute type, with at least some tendency toward vesiculation and exudation; the eruption should be symmetrical in distribution and more generalized, and pruritus should be a prominent symptom. A positive reaction to trichophytin should be a constant finding; fungi should not be recovererable from the lesions in culture nor visible microscopically in direct smears or histopathologic preparations, and the lesions should spontaneously involute after an acute course, provided the primary focus is found and eliminated. None of these characteristics was seen in this series of cases, and the evidence seems overwhelmingly in favor of an entirely different mechanism.

C. *Relationship to Majocchi's Granuloma Trichophyticum.*§—Beginning with the classic description by Majocchi in 1883,[6] this subject has been essayed several times in the Italian literature,‖ principally by his students. It is interesting to note that Majocchi himself wrote five additional papers dealing with this disorder.¶ The last one, in 1926, was written 44 years after his first memorable report. Additional contributions have appeared occasionally in various languages,# but the subject has been only rarely discussed in English.* From a careful survey of this literature the following concept of the entity has been derived.

In general, Majocchi's trichophytic granuloma consists of intracutaneous and subcutaneous chronic granulomatous nodules which arise within the confines of a plaque of dermatophytosis of variable type, without gross evidence of associated bacterial infection. The incidence is usually highest in childhood, although cases have occurred at all ages. The scalp is the usual site, although the beard, hand, scrotum, buttocks, and other, more generalized, areas of the glabrous skin have been involved. The nodules are almost painless; only slightly tender on pressure; duskily erythematous; usually discrete but occasionally grouped, without actual

§ Linguistic assistance for this portion of the study was given by Drs. M. E. Obermayer, Paul J. Catinella, and Lucille K. Georg. Mimeographed copies of translations into English of four of the most instructive of the papers (References 6, 31, 33, and 34) will be supplied by the authors on request.

‖ References 7-19.

¶ References 20-24.

References 25-37.

* References 38-42.

coalescence, and tend to occur near the more active border of the plaque. They show no acute features but always appear and disappear very slowly during several months. They are never the seat of grossly visible pustulation or abscess formation, but a pink or yellowish fluid may exude or be expressed. Many of them finally subside spontaneously by absorption, leaving no mark; others become necrotic in their centers, pursue an extended course, and eventually heal, leaving circular scars, either atrophic or, at times, keloidal. The nodules may long outlast the superficial trichophytosis.

Each nodule apparently arises from an infected hair follicle which fails to discharge the infected hair-shaft. Either because the hair turns back upon itself and by continued growth punctures the follicular wall mechanically or because an erosion of the follicular wall occurs from the pressure exerted by a microabscess, fungous elements are forced into the corium and incite a chronic granulomatous reaction characterized by epithelioid cells, small round cells, and occasional giant cells. Sabouraud, perhaps the most astute observer of all, believed that in all instances these fungus elements are accompanied into the corium by hairs, hair fragments, or at least cells derived from degenerated hairs or keratin material from the follicular walls.[31] Also, Sabouraud was convinced that none of the dermatophytes could live and proliferate in the corium without the nutritional support of such adventitiously derived keratin.

In most of the early reports the intracutaneous reaction to trichophytin was not determined; subsequent observers have reported the reaction to be frequently negative, sometimes mildly reactive, and only rarely highly positive, although Negroni and Bosq[43] were convinced that the syndrome represented an allergic trichophytid reaction. The fungi which were implicated were usually of the endothrix type (T. violaceum, T. cerebriforme, T. regulare, T. tonsurans), but an ectothrix fungus (T. gypseum) was thought by Sabouraud to have been the cause of a case reported by Pini.[8] In the case reported by Morikawa,[36] T. purpureum (rubrum) was isolated, but the disease presented by this patient was so widely disseminated, the "nodules" so very large, and the patient so profoundly affected that it is difficult to avoid the conclusion that some other pathologic process was concomitantly present. T. rubrum was definitely the cause of granulomatous nodules in the bearded area in the case reported by Harris and Lewis,[44] although the disorder was more pustular than that seen in our cases and was superimposed upon psoriasis.

It is apparent that the nodular granulomatous perifolliculitis exhibited in the presently reported group of cases bears a close relationship to Majocchi's "granuloma trichophyticum" and should in all probability be considered simply as a variant thereof. Several discrepancies must be pointed out, however. In our cases the disease has always been limited to the lower two-thirds of the area between the ankle and the knee. In all but two cases the infection was exhibited in one leg only. Our patients were all adult dark-haired women. Lastly, T. rubrum has thus far been the only organism observed.

D. *Differentiation from Other Entities of Fungal Origin.*—Under the designations "trichophytosis follicularis" or "lichenoid trichophytosis" Jadassohn[45] and Guth[46] described an eruption consisting of infiltrated papules occurring in connection with plaques of superficial trichophytosis, characterized by a lichenoid

prominence of the mouths of the follicles in the form of small coniform swellings. Jessner [47] considered this to be a terminal stage of superficial trichophytosis rather than a transition toward the development of granulomatous nodules. In most, if not all, these cases the "papules" were allergic trichophytids, as was also the case in those reported by Rasch [48] and Williams.[49]

The cases in epidemic form reported by Fisher [50] to be caused by T. gypseum (granulosum) seem to conform to the type of Majocchi's granuloma trichophyticum, although they were milder, by virtue perhaps of resulting from the invasion of lanugo hairs. In any event, nodular follicular and perifollicular infiltrates developed in the areas involved in dermatophytosis; these ran a chronic course, showed no tendency toward pustulation or bacterial infection, and persisted longer than the superficial process.

Differentiation from Nonmycotic Disorders of the Legs Characterized by Nodose Lesions

The presence of nodular lesions of varying size is a characteristic of several disease syndromes which frequently involve the legs. The most important aid in differentiating all these from the disorder exhibited by our patients is based upon the demonstration of the fungi which are the cause of the latter. It must be admitted that our present knowledge does not exclude the possibility that at times a fungus infection such as this may be secondarily superimposed upon tissues previously rendered less resistant because of some other disease process associated with nodules; indeed, it is to be hoped that further studies in this direction may explain some of the etiologic oddities we have encountered. However, we have not as yet been able to demonstrate any such relationship conclusively in any instance; much less are we able to suggest any such mechanism as a necessary characteristic. At this time, therefore, the discovery that T. rubrum is demonstrable in the deeper portions of a chronic nonsuppurative nodule existing within the confines of a plaque of dermatitis may be considered conclusive evidence that the disease belongs in this classification.

Our experience indicates that in most instances this syndrome is associated with an invaluable clue, which is easily obtainable by searching for evidence of T. rubrum infection elsewhere on the body. Several cases showed unmistakable clinical evidence of such involvement in toe or finger nails; typical hyperkeratotic lesions on soles and/or on one or both palms were sometimes present also. In a few instances it was possible to extract hairs from within nodules and to discover fungi in them by direct examination. Scaliness of the plaque of dermatitis with which the nodules are characteristically associated is an important clinical clue, and fungi are usually easily demonstrable in such scales. As a rule, direct examination or cultural studies may be relied upon to disclose the organisms in material from at least one of these sources if fungi are causative.

The final proof of the fungus nature of the nodules, however, must depend on the demonstration of the organisms within the nodules themselves. If it is established as a routine that all biopsy specimens from such lesions are searched for fungi by appropriate cultural and histopathologic methods, it is unlikely that any such cases will be missed. In all our cases in which biopsy was performed, the implantation on Sabouraud's medium of portions actually cut away from the sides of the deeper part of the specimen yielded colonies of T. rubrum. In some cases

histological specimens stained with hematoxylin and eosin revealed clumps of fungus elements; usually, however, the Hotchkiss-McManus method of staining was necessary, because of the sparsity of the organisms.

In general, a fungus infection of this type is unlikely to be the cause of a process exhibiting (1) nodules or ulcers larger than a centimeter in diameter or (2) more than a minimum of suppuration. The presence of (3) irregular areas of scarring larger than a centimeter in size also contraindicates it.

With regard to clinical features, if we limit erythema induratum (Bazin) sharply to those cases classifiable as tuberculosis cutis indurativa as recommended by Montgomery, O'Leary, and Barker,[51] the procedures by which the tuberculous etiology is proved should simultaneously deny the presence of fungi, although positive proof of the presence of tuberculosis may be delayed for several months.[52] The sarcoid of Darier-Roussy is closely allied to this syndrome; in both, the necrotic and ulcerative processes extend much deeper and wider and assume more bizarre shapes than in our cases. The lesions of nodular nonsuppurative panniculitis (Weber-Christian) are characteristically much larger and deeper and prefer the trunk and thighs.

Among the disorders based upon vascular insufficiency, the condition called pernio (chilblain), as described by McGovern and Wright,[53] is usually bilateral and presents painful lesions on the legs of adolescent girls, consisting of nodules which (1) are precipitated by exposure to cold and tend to disappear in the summer; (2) ulcerate frequently, yielding a purulent or serosanguineous exudate, and (3) exhibit a predilection for the internal malleoli and calves but frequently involve the toes and feet as well. The disorder described by Whitfield as multiple inflammatory nodules of the hypoderm[54] occurred in women from 30 to 40 years of age and consisted of painful nodose lesions on the legs, which recurred frequently, seldom ulcerated or produced scars, and tended to improve with bed rest. The condition called erythrocyanosis by Telford[55] is similar, but ulceration is less frequent and less extensive; sympathectomy cured almost all his cases. We have not seen cases which seem to belong in the category of periphlebitis nodularis necrotisans, as described by Bechet[56] and Philippson.[57] The excruciating pain which was said by Gonin[58] to have been characteristic of what he named ulcerating white atrophy of the leg has not been present in our cases nor has the history of varicosities or phlebitis nor the appearance of punctiform angiomatous formations. The entity called primary recurrent idiopathic thrombophlebitis by Barker[59] occurs almost always in men; the nodules are discrete but occur in crops, are linear instead of circular to palpation, extend along veins, are very tender, endure only for one to three weeks, and present no ulceration, necrosis, or scarring. Periarteritis nodosa could not be expected to remain as localized as the lesions were in our cases and would present a greater multiplicity of symptoms and signs.

In the cases reported by Traub and Tolmach[60] and Sulzberger, Rostenberg, and Goetz[61] as recurrent erysipelas-like manifestations of the legs, the patients were mostly men who sustained sudden attacks of redness and swelling at intervals of about two months, which were thought to be associated allergically with dermatophytosis of the feet; trichophytin testing did not, however, confirm a dermatophytid as a possibility in all. Similar to these were the patients of McGlasson[62] and Waisman,[63] as well as the cases of lymphedema of the extremities reported by Allen.[64] Nodules were not described in any of these entities, and there is apparently no simi-

larity with our cases. Although T. rubrum was implicated, the causative relationship claimed to exist allergically between trichophytosis of the feet and thromboangiitis obliterans, phlegmasia alba dolens, phlebitis migrans, and thrombophlebitis by White,[65] Thompson,[66] Naide,[67] and Thompson [68] seems not to be of importance in our cases.

The most difficult syndrome of all to differentiate by clinical means alone from our cases is that called nodular vasculitis by Montgomery, O'Leary, and Barker [51] and later by Wolf [69] and by Irgang.[70] In fact, this had been the diagnosis applied to several of our patients previous to the clarification of the fungus cause, both by ourselves and others. Indeed it seems likely that mycologic investigation may reveal a similar fungus etiology in at least some cases such as these, especially when the nodules are small and do not ulcerate extensively. The evidence of venous stasis has not been present in our patients, and unilaterality has been a more constant feature; there was also less evidence of obliterative changes in the vessels histopathologically. The principal reliance here must be on the definitive search for fungi. In the discussion of the paper of Montgomery, O'Leary, and Barker [51] Weidman † stated, "In future studies of nodular vasculitis one should check for the presence of dermatophytosis," a dictum which we strongly advocate. It is not to be expected that this syndrome will explain all or even any great percentage of such cases, but the possibility of clarifying the etiology in even a few instances warrants routine mycologic investigation.

MYCOLOGY

The only organism thus far recovered from our series of cases of nodular granulomatous perifolliculitis has been T. rubrum (T. purpureum, Bang). The cultures have all been typical for this organism within its well-accepted limits of variation. No granular strains were discovered, all were profusely cottony, and pigment production was good.

By direct microscopic examination of extracted hairs the fungi were seen mostly as an ectothrix mosaic mantle of rather large spherical or oval spores. However, in most hairs an endothrix element was also present, consisting of short hyphal segments and chains of oval or rounded arthrospores longitudinally directed with relation to the hair shaft. This endothrix component was very evident in sections of biopsy specimens stained by the Hotchkiss-McManus method. This observation is in agreement with that of some observers ‡ and contrary to that of others.§ Rounded spores were also seen in the corium in the granulomatous areas; this phase will be described more fully in connection with the histology.

HISTOPATHOLOGY

Many authors have studied and discussed in detail the histopathology of Majocchi's granuloma trichophyticum, particularly Vignolo-Lutati,[30] Majocchi,[23] Mazza,[29] Oro,[16] Pini,[8] Pasini,[32] Sabouraud,[31] Sequeira,[40] and Ciaccio.[74] The histopathology revealed by the sections obtained from our patients seems to conform to the general picture and is especially similar to the illustrations in Sabouraud's "Les teignes," [31] which were taken from Mazza's case.

† Weidman, F. D.: in discussion on Montgomery, O'Leary, and Baker.[51]

‡ References 72 and 73.

§ References 74 and 75.

Serial sections made from several nodules taken from our patients reveal that each is composed of a mass of infiltrate around an infected hair situated within a follicle whose wall has undergone more or less necrotic destruction (Fig., *B*). The infiltrate is polymorphous and is composed of epithelioid cells, fibroblasts, giant cells, plasma cells, and lymphocytes. The reaction is predominantly chronic, but some areas show small acute microabscesses crowded with polymorphonuclear leucocytes and numerous eosinophiles (Fig. *Ba*). Various degrees of cicatricial healing have been observed. The epidermis is either unchanged or somewhat flattened by pressure from beneath; fungal elements may sometimes be seen in the stratum corneum.

We agree that each nodule arises as the result of the involvement by the fungus of a hair within its follicle, from which source in some way the organisms come to lie within the cutis beyond the confines of the follicular cavity and wall. Sabouraud [31] was convinced that this process occurs by one of two methods; either that a hair becomes turned backward on itself because its outlet is sealed off and, by continuing to grow, finally punctures downward through the follicular wall, thus mechanically pushing infected hair substance into the corium, or that, as the result of pressure of a minute abscess, a necrosis of the follicular wall occurs, leading to the forceful extrusion of the contents of the abscess into the corium. We have seen no evidence of the former mechanism, but the latter seems to be typical. However, Sabouraud also stated his belief that the fungi could not live and proliferate in the corium without depending for nutrition upon keratin derived either from hair shaft fragments or follicular wall debris which is carried along with them as they are transferred, while others (Pellizari,[25] Sorrentino,[13] Chirivino [14]) believed that the fungi could actively emigrate under their own power into the corium and proliferate there. In some of our cases we have seen large masses of fungi in the corium, in an apparently healthy condition, far removed from any demonstrable keratin material. As has been mentioned before, some fungus cells are much larger than would be ordinarily expected and stain less intensely; this occurs particularly where they are sparsely distributed (Fig., *D*). This may, of course, mean that they are swollen in the process of degenerating rather than that they are extraordinarily well nourished; however, we have seen no evidence of fragmentation, pyknosis, or vacuolization, as described by Sabouraud,[31] to confirm this view. It must be admitted that fungi are not seen in healthy corium and that necrotic material is present in all involved areas; consequently, the view that they cannot thrive by digesting living tissue may still be valid. However, such deviations of the corium as are seen may easily be the direct result of the activities of the fungus; at least no other mechanism has as yet been apparent to account for them.

The vascular changes found by Winer [75] to be so characteristically present in some diseases producing nodose lesions in the legs were not seen in any of our cases.

EPIDEMIOLOGY AND PATHOGENESIS

As has been reported [1] T. rubrum is encountered frequently in southern California as a cause of dermatophytosis; the incidence seems to be much higher than in most other localities. Thus it is to be expected that the disorder under discussion will also not occur as frequently elsewhere as here.

Among the various manifestations of this infection, dermatologists in southern California have long been aware of a peculiar nonpustular form of folliculitis caused by T. rubrum and occurring usually on one or both legs of dark-haired women either with or without similar infection elsewhere. Such cases have been slow to respond to therapy and prone to recur. It is evident that the formation of perifollicular granulomatous nodules as described here is but a step further in this process, resulting from a penetration of the organisms deeper than the follicle itself. It seems likely that the process of shaving the legs may account for the location of the disease between the ankles and knees as well as its predominance in dark-haired women, who find the hairs more objectionable cosmetically. In this regard it is interesting to note that, in 1922, Davidson and Dowding [76] attributed the newly observed phenomenon of tinea barbae on the upper lip as due to the fact that moustaches had largely gone out of style. The larger diameter of the hair shafts and the size of the follicles in persons with dark, coarse hair may also be a factor; many of these legs are covered with what can hardly be called "glabrous" skin. The fact that the disorder is found only in adult women, most of whom are young and none long past the menopause, may signify that some glandular influence connected with menstruation is influential. So far no case has occurred during pregnancy. In other forms of dermatophytosis caused by this organism, however, men are predominantly affected.

There has been no lowering of the blood-sugar-tolerance curve observed in the four cases in which such tests were employed; thus the influence of this factor, which was stressed by Rothman,[77] was not apparent. Neither was there any evidence of leukemia or other lymphoblastomata in six patients tested, as suggested by Lewis.[78] Psoriasis was not present in any of our cases, as it was in the case reported by Harris and Lewis.[44] There was no eosinophilia of the blood nor any large concentration of eosinophiles in the nodules, as in the case reported by Lewis and Cormia.[79]

We adhere strongly, however, to the concept that some immunologic or biochemical mechanism as yet poorly understood exerts a controlling influence upon the epidemiology and pathogenesis of T. rubrum infections. None of the proposals previously mentioned explains the bizarre tendency toward unilaterality so frequently observed in the present series of cases as well as in other forms of dermatophytosis caused by this organism,|| especially when there is involvement of the palm or, less frequently, the sole. Persistence in this unilaterality has continued in some cases for years.

Although it was formerly thought that T. rubrum seldom if ever parasitizes the hair, Ota [83] as early as 1922 pointed out that this organism was encountered frequently as a cause of tinea capitis in Japan, and Milochevich [84] reported a case of sycosis in 1935. Also, even though we believe Anderson's case, in 1941, to have been similar to ours, it is strange to find so many cases which indubitably fall into this classification suddenly appearing within two years. It seems unlikely that this sudden increase in incidence can be due entirely to a heightened index of suspicion as to mycologic disorders or to the advent of the wonderfully helpful Hotchkiss-McManus stain, as advocated by Kligman and Mescon.[85] It is more reasonable to

|| References 80-82.

conclude either that T. rubrum is becoming more virulent or that some change is occurring in the bodies of a significant number of persons leading to their infection by this organism. In this regard we call attention to the recent reports by several authors on kerion being caused by T. rubrum ¶ as well as other bizarre activities of this organism reported by Levin and Behrman,[88] Salzar Leite and Bastos da Luz,[89] Baer and Muskatblit,[90] and Costello.[91] That T. rubrum (at least the strains being recovered during recent years) may differ from other dermatophytes in being able to proliferate at the expense of living tissues, even those of the viscera, is indicated by the recent work of Sternberg, Tarbet, Newcomer, and Winer.[92] Perhaps further studies, such as those by Reiss [93] and Wharton, Reiss, and Wharton,[94] may clarify the immunologic phases of infections caused by this organism.

THERAPY

The selection of therapy was guided by experience gained in the treatment of the kerion-like deep infections caused by T. faviforme and T. mentagrophytes usually acquired from contact with cattle or rabbits. In these cases potassium iodide, given orally to the point of maximum tolerance, combined with mildly filtered x-radiation in fractional dosage and some type of fungicide applied locally, had proved efficacious. Because of our conviction that 2-dimethylamine-6-(β-diethylaminoethoxy)-benzothiazole (Asterol) dihydrochloride is at present the most effective topical medicament in chronic dermatophytosis caused by T. rubrum,[80] this drug was selected as the fungicide in all cases under our supervision, utilizing the 5% "tincture" twice daily as a spray which was allowed to dry, followed by the application of the 5% ointment. X-radiation was employed at intervals of from one to two weeks, using 75 at 85 kv. filtered with 1 mm. of aluminum. Potassium iodide was given either as the saturated aqueous solution or in enteric-coated tablets; a dosage of 45 to 60 grains (3 to 4 gm.) daily was usually tolerated well.

Under this combined treatment the response has usually been satisfactory, although from 6 to 16 weeks have been required to effect a cure. In Case 1 intolerance to Asterol developed after 12 weeks, manifested by a vesicular erythematous contact dermatitis; patch testing confirmed this allergic state. The original disease had been improved almost 90%, however, and subsequent use of 1% iodine ointment resulted in complete clearing. One patient stated at the outset that she was unable to tolerate iodide, having attempted unsuccessfully to take strong iodine solution, U. S. P. (Lugol's solution) some years previously; she sustained a severe attack of hay fever and asthma on each of three occasions when we urged her to attempt to utilize it for the present disease. It is deemed significant that the iodide is an important part of the therapy because of the fact that this patient has sustained recurrence of the nodules twice after the condition was apparently controlled, whereas other patients have not. Since, in her case, x-radiation has also been utilized, to the advisable limit, she has been attempting to avoid further recurrence by applying the fungicide once or twice weekly for an indefinite time. A recurrence consisting of three nodules has occurred during this therapy.

In several cases the T. rubrum infection has remained active in toenails or soles after the lesions on the legs have been cleared, and recurrence of nodules seems

¶ References 73, 86, and 87.

likely unless some therapy is continuously employed. We are now advising all patients to apply a fungicide locally at intervals of a few days for long periods of time, especially immediately after shaving the legs, if such a practice cannot be entirely avoided. For this purpose Asterol in tincture form as a spray seems to be effective, well tolerated, and appreciated.

SUMMARY

In California, during the past two years, 14 cases have been discovered in which nodules composed of a chronic granulomatous infiltrate surrounding infected hair follicles have been prominently displayed within the confines of plaques of scaly erythematous trichophytosis usually distributed unilaterally on the lower portions of the legs of dark-haired women.

Trichophyton rubrum (purpureum) has been uniformly recovered in culture from material removed superficially from the areas of dermatophytosis as well as from the sides of the deeper portions of specimens removed for biopsy. Histopathologic preparations stained by the Hotchkiss-McManus method revealed fungus elements in hair shafts as well as in the midst of chronic granulomatous areas in the corium.

Clinically and histopathologically the process closely resembles Majocchi's trichophytic granuloma in many respects. The location and distribution of the disease and the causative organism are different, however, as is the tendency to unilaterality.

Therapy has been successful in controlling the disease in most instances, using potassium iodide orally, mildly filtered x-radiation locally, and topical applications of 2-dimethylamino-6-(β-diethylaminoethoxy)-benzothiazole (Asterol) as a fungicide in both tincture and ointment form.

Recurrence is to be expected in many instances because foci of trichophytosis remain uncured in nails, soles, or other areas, and there are unknown factors in the pathogenesis and epidemiology of T. rubrum infections which render certain persons abnormally susceptible.

ABSTRACT OF DISCUSSION

Dr. James Lewis Pipkin, San Antonio, Texas: Dr. Wilson has rendered another service to us by bringing to our attention this unusual and bizarre clinical manifestation of Trichophyton infections of the skin. The reported cases were due to Trichophyton rubrum, but I am firmly of the opinion that other trichophytons can produce such a clinical picture.

Our interest in this type of infection was stimulated by Dr. Wilson's experience, cited to us some 18 months ago, and since that time we have observed two patients with similar chronic lesions. One such instance was due to Trichophyton tonsurans (crateriforme group), which was inoculated into the posterior surface of the lower third of the leg by the young lady's finger nail. In pulling up her stockings, she scratched her Trichophyton-infected nail along the posterior surface of her leg and developed this bizarre lesion, that fitted very well into this described picture.

The other instance of such a deep nodular trichophytosis was that of a woman who probably contracted the infection on the posterior surface of her leg by shaving with her husband's razor. The original fungus infection in this family was contracted by a child, who presented a classical kerion. The father later contracted the infection in his beard and presented a massive trichophytic granuloma. On first sight, we thought the organism was Trichophyton mentagrophytes, owing to the apparent location of the spores, but upon careful study with cultures we found an unusual red organism. We interpreted this as a Trichophyton mentagrophytes with a peculiar red coloration. Dr. Lucille Georg was kind enough to aid us with this problem and, after

extensive study, decided that the organism was Trichophyton rubrum and that the spores were not only located on the inside of the hair but were also on the outside of the shaft. In other words, we were dealing with a neoendothrix type of infection.

Both these patients were very hairy people. This fact may help to account for this peculiar lesion.

In establishing the etiology of such atypical lesions, two points are worthy of mention. I grant you that they are elemental, and I should probably be criticized for mentioning them. However, this technique is not used commonly in usual office procedure. The first point is the use of multisites for the selection of material for fresh hydroxide examinations and for cultures. It is not unusual for us to make as many as six or eight cultures and hydroxide mounts and isolate a pathogen on only one of the eight. If one happens to select an area from which one fails to pick up the organism, one misses the diagnosis, either by culture or by the examination of the fresh material. The second point of importance in aiding one to establish the diagnosis in these bizarre eruptions is the removal of a large piece of skin with adequate depth. In other words, to secure proper material for cultures and fresh hydroxide mounts in these deep fungus infections, one removes tissue much in the same fashion as in taking a biopsy specimen, oftentimes resorting to the use of procaine (Novocain).

Dr. Jacob H. Swartz, Boston: It seems that the final chapter on the micro-organism known as Trichophyton rubrum has not yet been written. I recall my early days in mycology, at the Massachusetts General Hospital, when the finding of T. rubrum on culture from skin lesions was occasion for excitement, since such a finding was rare. Weidman, in 1927, and Lewis, in 1930, stated that this was an uncommon fungus in the northeastern part of the United States. Since then the fungus has frequently been found, involving the feet, hands, and nails. Occasionally, even the hair is involved.

In the last two decades T. rubrum has been reported to be capable of producing widespread and bizarre cutaneous lesions by Lewis, Montgomery and Hopper, Muskatblitt, Ayers, Swartz and Conant, and others. Recently Lewis, Hopper, and Scott described a generalized infection associated with systemic lymphoblastoma.

In 1930 Harris and Lewis reported a deep granulomatous lesion on the neck from which the fungus was isolated from the pus, the hairs in the granulomatous area, and the macerated skin on the feet.

In 1937 Morikawa described an extensive eruption consisting of superficial papules and subcutaneous nodules. T. rubrum was recovered from the superficial and the deep lesions.

Reiss, in 1944, and Sternberg, Tarbet, and Winer, in 1952, reported successful inoculation of rabbits with T. rubrum, resulting in granulomatous lesions. Now Dr. Wilson reports granulomatous lesions on the legs.

Several interpretations of Dr. Wilson's cases present themselves. The first is that the fungus was transplanted from another focus to a locus minoris resistentiae on the legs, where an original nonmycotic disease, such as nodular vasculitis, was present. Dr. Wilson has considered this possibility. In a case of dermatitis nodularis necrotica in a patient with severe diabetes I cultivated T. rubrum from the skin scrapings. Histologic examination of the granulomatous tissue did not reveal fungus elements when it was stained with the usual tissue stain. This was before Kligman and Mescon reported the Hotchkiss-McManus stain for fungi in tissue. The patient also had onychomycosis caused by T. rubrum. I believed at that time that the fungus was transplanted to an area of lowered resistance. I did not think that the granulomatous reaction was due to T. rubrum. I might have a different opinion now.

At the Massachusetts General Hospital there is a young woman wtih pemphigus vulgaris who developed papules and pustules on the upper and lower extremities. She also showed on the extensor surface of the left forearm two nontender nodules, each measuring 1 cm. in diameter. Histopathologic examination of a sectioned nodule showed localized microabscess formation and giant cells, some containing spores and few mycelial fragments. The Hotchkiss-McManus method of staining was used. Material from the pustules stained by the Hotchkiss-McManus method revealed spores and septate mycelia. T. rubrum was grown from the granulomatous material. Both the superficial and the nodular lesions healed completely without treat-

ment within three weeks, leaving hyperpigmentation and depressed scars. The patient had long-standing tinea pedis caused by T. rubrum. This patient had a good deal of antibiotic therapy, which may have been a factor.

The second explanation is that one may be dealing with a more virulent strain, which, unlike the usual strain, at first produced an acute inflammatory reaction but which, because of the persistence of the lesion in a location where hair follicles are present and the lack of immunologic response on the part of the host, changed in character to that of a chronic granuloma, similar histologically to the reaction induced by less virulent strains. Sabouraud's finding of suppuration, at least microscopically, in the early stages of trichophytic granulomas and the presence of acute microabscesses in Dr. Wilson's cases and the case at the Massachusetts General Hospital support this theory.

A third possibility is that the infection began as a superficial one in the epidermis, extended to the hair follicle, and finally reached the cutis by one of the processes that Dr. Wilson describes. As the follicular epithelium or hair substance diminished, the fungi adapted themselves to their new environment and metabolized substances other than keratin. The probability that the dermatophytes in time of need can metabolize substances other than what they are used to was suggested by Rothman in an excellent paper entitled "Systemic Disturbances in Recalcitrant Trichophyton Rubrum Infections."

Dr. Wilson mentions that, in addition to the finding of ectothrix mosaic arrangement of chains of roughly spherical spores, chains of spores together with short hyphal segments were situated within the hair shafts. The finding of chains of spores within the hair shaft is interesting, since T. rubrum is considered to be a large-spored ectothrix.

The report in this paper of good therapeutic results with potassium iodide by mouth coincides with my experience in the treatment of the recalcitrant superficial infections due to T. rubrum, except that I have administered an organic iodide (ethyl iodide) by inhalation. This treatment has proved even more effective than the oral administration of potassium iodide.

In conclusion, work such as that reported by Wilson, Lewis, Hopper and Scott, Sternberg, Tarbet and Winer, Reiss, and others will in time write the final chapter to the story of T. rubrum.

Dr. Samuel Ayres Jr., Los Angeles: I think we are rather proud of Walter Wilson for wrapping up this rather neat package for us in the manner in which it has been done and calling attention to an entity which certainly has escaped attention.

We have, during the past seven years, encountered six cases, I think, which are this same entity, in women. I don't know whether they were light- or dark-haired. In four of them we were unable to obtain cultures; that is, they were overgrown and contaminated; in two of them Trichophyton rubrum was obtained, and in all of them the fungus was found by direct examination of the hairs or scales or both. In three of these patients we encountered characteristic lesions on the feet.

In addition to these six definite cases in women, there is at least one other patient with lesions that are more extensive and look almost like bromide granulomas, in whom we found the organism by direct microscopic examination, but so far we have been unable to obtain positive cultures or duplicate our original findings.

In addition to this, we have seen two children, two boys aged 3½ and 8 years, who had similar lesions on the leg, but in whom we found Microsporum fulvum. Then, of course, we have encountered other instances of tinea-profunda-type lesions in four men, in different locations of the body. I have simply diagnosed all of these as tinea profunda, but I think that the type of lesion which Dr. Wilson has described could be classed as an entity. Considering the fact that T. rubrum is quite an imitator, it is probably a good idea to take scrapings for microscopic examination and cultures in cases of eruptions which are atypical.

Dr. George C. Andrews, New York: I also enjoyed Dr. Wilson's paper. I have seen cases similar to these. We had one patient with an eruption of the unilateral type on one ankle. It was an eczematous type of eruption, with very superficial scaling. From this we grew Trichophyton rubrum, and nothing else could be shown in other parts of the body or feet.

We had another patient from whom we got an endothrix from the hair on the leg, with a nodular lesion similar to the one shown on the screen. Then we had a patient who had an

eruption that looked like widespread keratosis pilaris and folliculitis of the extremities and trunk, itching intensely. I had no idea that it was a fungus infection. I thought she might have scabies. We could not demonstrate the acarus. I gave an ointment for scabies, and the next week she insisted that the eruption came from a cat that they had. Scratch test to cat hair was negative. Her husband had the same sort of thing on his legs. She brought him in. We looked for a fungus and found it immediately. It turned out to be Microsporum canis. She said five or six other people had gotten it from the same cat and had the same type of eruption. I couldn't get her to bring in the other people, but she and her husband both had this follicular type of eruption from M. canis, which is unusual.

In this connection, I would like to mention that Aldo Castellani, who died a month or two ago, described lesions due to a fungus called Acladium castellani, or acladiosis, which resembled erythema nodosum, from the lesions of which he got rather large spores and hyphae. I wonder whether his acladiosis has anything in common with the cases described by Dr. Wilson.

Dr. Maximilian E. Obermayer, Los Angeles: I should like to tell you in a few words about the circumstances of the rebirth of Majocchi's granuloma. The first patient was referred to Dr. Wilson by a specialist in the treatment of vascular diseases, with a statement that, in his opinion, the disorder was not vascular. Dr. Wilson examined the patient and informed her of his intention to perform a biopsy and to plant cultures.

I then examined the patient, at his request, and my impression was that the lady had nodular vasculitis. Dr. Wilson was willing to accept the diagnosis, but he stubbornly insisted on biopsy and cultures, perhaps because he was reluctant to tell the patient that he had changed his mind as to their necessity. Instead of betting the usual nickel, as is our custom in the office in problems of differential diagnosis, I just threw up my hands and said, "If that's of fungus origin, I'll take my shingle off the wall." I was wrong, but I did not take my shingle down.

This experience has taught me how fallacious it can be to rely on clinical acuity alone. Had it not been for Dr. Wilson's insistence, it would have probably taken a long time to revive awareness of this granuloma, and when you consider that there are at least 14 cases now known of this important entity in southern California, you realize that he has made us all conscious of its presence, and I can only congratulate him on his careful and brilliant study.

Dr. J. Walter Wilson (Closing): I wish to thank the discussers, Drs. Swartz, Pipkin, Ayres, Andrews, and Obermayer, for their considerate remarks. The disease called acladiosis, which was reported by Dr. Castellani, was caused by a dark-colored fungus, the hyphae of which would appear brown both in the direct examination of potassium hydroxide preparations and in histopathologic sections. There could therefore be no difficulty in differentiating that fungus from the present organism, Trichophyton rubrum.

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CONTRIBUTIONS OF EXPERIMENTAL ANIMAL RESEARCH TO DERMATOLOGY

J. LAMAR CALLAWAY, M.D.
AND
GEORGE W. HAMBRICK Jr.
DURHAM, N. C.

AS NOTED by the title, the scope of this paper is profound. It is impossible to list all the contributions. The efforts reported in this paper are concerned primarily with the reports from two journals, the A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY and the *Journal of Investigative Dermatology*. From 1932 through 1952 there were approximately 90 articles concerned in some way with small animal experiments reported in the former journal and 100 articles in the latter journal from 1938 through 1952.

Farris, who edited a book entitled " The Care and Breeding of Laboratory Animals," in 1950, presented the following statistical data:

The selection of the species to be included in the book was based primarily upon the results of a survey of animals used by American investigators, or determined by papers presented at annual meetings of three representative scientific organizations: The American Association of Anatomists, The American Society of Zoologists, and the Federation of American Societies for Experimental Biology which includes the following groups: The American Physiological Society, Inc., The American Society of Biological Chemists, Inc., The American Society for Pharmacology and Experimental Therapeutics, Inc., The American Society for Experimental Pathology, The American Institute of Nutrition, and the American Association of Immunologists.

The species employed in 1,500 investigations in 1947 are listed in order of frequency of use, as follows:

Mammals:			
Man	334	Pig	8
Rat	317	Horse	4
Dog	258	Others	16
Rabbit	110	Aves:	
Mouse	108	Chicken	58
Cat	81	Other Fowl	12
Guinea Pig	49	Amphibia	59
Monkey	41	Reptiles	2
Cow	25	Fish	21
Hamster	9	Invertebrates	118
Sheep	9	Not stated	32

From the Division of Dermatology and Syphilology, Department of Medicine, Duke University School of Medicine.

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Rothman, in his presidential address to the Society of Investigative Dermatology in 1949, stated the problems encountered in the carrying out of animal studies:

> Our second inherent difficulty lies in the fact that the structural differences between human and animal skin are much greater than the differences in any other organ. One can speculate that in the phylogenetic development the human tegument, similar to the olfactory organ, has been degenerating. It certainly has lost its hair and in the white races also most of its pigment.
>
> Not only structurally but etiologically, too, the differences are sufficiently great to make animal experimentation difficult. In most animal species it is not possible to produce blisters or wheals, and only in a few species can the skin be sensitized in the same fashion as in man.
>
> A third great obstacle is that only a very few human skin diseases can be transferred to animals.

STUDIES OF EPIDERMIS

The studies of pH of the skin of man and common laboratory animals revealed that the pH of man (4.04 to 6.26) is slightly lower than that of guinea pig (4.26 to 7.17). Pig embryo skin has been studied with regard to the histogenesis of the epidermis.

Thuringer studied the mitotic index of the epidermis, using palmer and plantar pads of cats. In response to stimulation, the peak in the number of mitoses reached was found to occur two hours after stimulation. The majority of the mitoses were in the stratum germinativum, but the basal layer also participated.

In doing homografts in white rats success depended on using young donors; autografts using thin grafts were successful, but did not produce good hair growth.

A report concerning the production of bullae in duck skin with sensitization was made by Goldman. The concentration of sulfonamide in the bulla was found to be in equilibrium with that in the blood plasma. In guinea pigs application of iodoacetic acid in 5 to 10% concentration produced vesication.

Several authors have studied the permeability and absorptivity of the skin in various species. Monkeys as well as humans have been shown capable of absorption of proteins percutaneously. Animal fats penetrate unbroken skin of rabbits through the hair shafts and oil-gland ducts in the descending order. The peak penetration occurs four to six hours after application. McKee and co-workers showed the best penetration to occur with water propylene glycol, interface active agents, coupling agents, and solubilizers. The route of penetration was down follicles into sebaceous glands, thence into the cutis or up outer root sheaths, and also upward from the cutis to the basal-cell layer to a color-free band zone corresponding to the stratum lucidum. Sweat ducts are of no importance in absorption.

Epidermal absorption with use of diethylene glycol monoethyl ether (Carbitol) as a vehicle was demonstrated for epinephrine, penicillin, and choline esters in rabbits, while insulin was not absorbed. A study of the hydrophilic absorption ointment bases showed no effect on wound repair in animals. The distribution of radioactive iodine in various organs of the rabbit and guinea pig after percutaneous absorption was studied. Grease bases and polyethylene glycol (Carbowax) were found to be efficient vehicles for external application of dimercaprol (British anti-Lewisite—BAL) in the rabbit.

Experiments using application of ointments containing sulfonamides to the skin of guinea pigs revealed that there was little relationship between penetration and the type of ointment base, that is, whether it was an oil-in-water or water-in-oil emulsion base. Above 1% concentration of sulfonamide had little effect on tissue levels of sulfonamide reached.

Cold-permanent-wave-process chemicals have been variously studied. Using the mouths of various species, ammonium hydrogen sulfide and hydrogen sulfide was absorbed to such a degree as to produce death in rabbits and mice. In another study, local application of bisulfite and thioglycolic acid to the skin of normal guinea pigs and rabbits resulted in changes which were demonstrable as soon as 30 minutes after application. Bisulfite produced mild reaction, but a three-hour application of thioglycolic acid produced extensive necrosis. A 6.5% solution of thioglycolate applied to rats and guinea pigs produced no ill effects in the hands of other investigators.

A method for separation of the epidermis of guinea pigs, rats, and rabbits using chloroprene dimers with subsequent exposure to freezing temperature and 50 C. heat is reported.

Estrogens by inunction increased epidermal proliferation in ovariectomized rats, while estrogen by injection produced quantitative thinning of the epidermis. Rhino-mouse skin was treated with estradiol applications, and this resulted in increased keratinization of the abnormal hair follicles, hyperemia of the skin, and involution of the cutaneous sebaceous glands. Ketohydroxyestrin applied to the skin of spayed albino rats in an oily vehicle is absorbed through the skin in sufficient amounts to cause estrus. Percutaneous application of estrogens in rabbits caused a reduction in size of the sebaceous glands and stimulation of the hair papillae, with an increase in rate of growth of the hair. Testosterone produced hyperplasia of the sebaceous glands and reduced activity of the pilar papillae. The effects were reversible.

A nipple test devised by W. Jadassohn and co-workers involved guinea pigs. Aqueous estrone solution produced enlargement, as did oily solutions of estrone in male animals; while aqueous testosterone propionate produced minimal enlargement, and oily solution produced no enlargement.

Hyperkeratosis beginning in the second week after thorium X application and persisting through the sixth week has been observed in rabbit skin.

Cormia and Bryan found that 1,600 r was an erythema dose in albino rabbits, using 110 kv., 7 ma., 20 cm. distance, and 1 mm. Aluminum plus 0.5 mm. inherent. The skin of rabbits on exposure to mild agents plus irradiation did not react adversely, but if 10% tar salve or 10% ichthammol (Ichthyol) salve plus irradiation were used a summation effect occurred and actual keratoses were produced.

Animal experiments have shown that excessive irradiation with a hot quartz ultraviolet lamp can produce cutaneous cancer, but there was little evidence that any clinical cases of cancer have followed the use of sun lamps. Experimentally, it was found that "mid-ultra violet" (2,967, 3,024, 3,132A.) energy necessary to produce skin cancer in the ears of 50% of white mice ranged from 672 to 2,360,000,000 ergs per square centimeter over an irradiation period of 135 days. Cold quartz mercury of 2,537 A. radiation produced no tumors.

HAIR

Hereditary hypotrichosis in the rat has been found to be caused by a single recessive gene. Experimental alopecia was produced in cats by removal of the ganglion of the second cervical nerve with its anterior and posterior roots bilaterally. This alopecia was limited to the occipital regions, ears, and throat areas bilaterally.

Several unsaturated compounds were tested for their local depilatory action in mice, guinea pigs, and rabbits. A single application of allyl laurate, allyl benzoate, allyl diphenylacetate, or squalene, and repeated applications of vitamin A caused reversible hair loss at the site of application. With the exception of vitamin A, these compounds inactivated in vitro the free sulfhydryl groups of glutathione and of tissue homogenates and the sulfhydryl enzyme succinic dehydrogenase. Local application of human sebum caused reversible hair loss in rabbits and mice. In general, the in vivo depilating ability of an agent correlated with its ability to inactivate sulfhydryl groups.

Templeton and co-workers performed a series of experiments and found that when gasoline containing 0.03% tetraethyl lead and 0.02% ethylene dibromide is applied to the skin of rabbits, rats, or guinea pigs, loss of hair results in the areas to which it has been applied, in varying degrees, lateral to the point of application. Regrowth of hair can be noted clinically in about three or four weeks and is complete in about seven weeks. If stronger gasoline containing large amounts of tetraethyl lead were used for a week, approximating one-fourth to one-third of the animals died. Control animals treated with kerosene and plain gasoline are not affected.

Subcutaneous implantation of 8 to 10 mg. pellets of crystalline androsterone, estrone, etc., but not testosterone propionate, was usually followed after varying periods by partial pigmentation of the fur of albino rats and by alopecia in a strain of dark gray-brown rats.

In studying the cystine content of hair of rabbits and guinea pigs dark hair was found to be higher in cystine, and it is thought this is associated with increased pigment.

PIGMENTATION

Many contributions have been made toward understanding pigmentation in humans. It is beyond the scope of this paper to elucidate this picture. In guinea pigs and mice monobenzylether of hydroquinone and *p*-hydroxypropiophenone are effective inhibitors of pigmentation both locally and parenterally administered. Small areas of black and white skin of guinea pigs were interchanged in the form of autogenous full-thickness grafts. When a pigmented graft was transplanted to an area of white skin the pigmentation would seem to occur in the host epidermis initially in the skin in contact with the graft. After this, pigmentation developed centrifugally in an irregular fashion for a distance beyond the graft margin. After transplantation of the white graft to the pigmented area, the graft became pigmented. White graft transplanted to white skin did not become pigmented.

Whale skin has been found to react similarly to human skin.

TUMOR PRODUCTION

Verrucae were found in man, cattle, dogs, and horses. Attempts to produce encephalitis with the filterable virus were unsuccessful.

Production of epidermal carcinoma in mice by application of methylcholanthrene has been studied extensively. The greatest mitotic activity occurred in the prickle-cell layer; chromosome enlargement was noted at 48 hours and increased to 13% at three days. Ribonucleic acid and alkaline phosphatase values were increased. Osteosis cutis occurred in one experiment subjacent to the anaplastic carcinomas

produced by methylcholanthrene. White mice easily developed epitheliomas over a six-month period after benzpyrine painting, while black and white mice infrequently developed epithelioma. Tumors were also produced by a single application of dimethyl 1:2 benzanthracene on mice. Examination of the internal organs of several thousand mice painted with carcinogenic agents in relation to individual susceptibility to tumor formation were carried out, without striking results.

EPIDERMAL SENSITIZATION

There are numerous reports of epidermal sensitization in the guinea pig to various substances, including poison ivy antigen, dinitrochlorobenzene, aromatic amines, dyes, and the arsenicals. Guinea pigs fed a low vitamin C diet were less sensitive to poison ivy, but when returned to an adequate vitamin C diet were as sensitive as normally fed animals. Rabbits were not easily sensitized to poison ivy. Guinea pigs could not be sensitized to orris root, giant ragweed, or sage. Sensitized guinea pigs were treated by various extracts of poison ivy by mouth and by intramuscular injections. The former route seemed to be more efficient as an immunity builder. Ginsberg and co-workers desensitized sensitive guinea pigs by repeated application daily of a ragweed extract—a process analogous to "hardening" observed industrially in humans. Guinea pigs previously sensitized to 2:4 dinitrochlorobenzene showed no greater tendency to become sensitized to ragweed than did previously nonsensitized animals. Histologically there was little similarity in degree to that demonstrated in humans, as guinea pigs do not vesiculate easily.

Attempts to sensitize guinea pigs to nail lacquers and brilliant green failed. In small groups of guinea pigs, severe artificial fever reactions as produced by the Hypertherm prevented the development of skin hypersensitivity to turpentine. Guinea pigs sensitized to phenylenediamine received total body irradiation of 175 r. An attenuation of the degree of skin sensitivity appeared in a majority of the irradiated animals as compared with the nonirradiated controls.

Rabbits were given injections of carbon tetrachloride to produce liver damage. There were no detectable differences in their ability to react to croton oil full strength applied locally.

Frei in a series of experiments inducing arsphenamine hypersensitiveness in guinea pigs found that the skin hypersensitiveness was directed toward the aromatic arsenicals in general and that vitamin A had no enhancing effect. Cormia was unable to elicit positive Schultz-Dale phenomenon with sera from guinea pigs suffering from experimental arsphenamine dermatitis. Concurrent infection with hemolytic Group C Streptococcus accentuated the manifestations of cutaneous arsphenamine hypersensitivity. A diet high in vitamin C inhibited the accentuation. Staphylococcus toxin did not influence the severity of the induced cutaneous hypersensitivity to arsphenamine, even when the diet was low in vitamin C. A variation in the vitamin C content in the diet ranging from 0.025 to 0.2 mg. of ascorbic acid (cevitamic acid) daily had little if any influence on the development of cutaneous arsphenamine hypersensitivity in guinea pigs.

Various investigators have attempted to show the route of spread epidermal sensitizations. Generalization of sensitization occurs even if the island involves cutting the skin and lymphatics. Haxthausen sensitized guinea pigs to dinitrochlorbenzene by a single application to the shaved skin. A peritoneal exudate was produced by intra-

peritoneal injection of a 2% agar solution. The washed cells of this exudate were injected intraperitoneally into nonsensitized guinea pigs. One to four days later these receptor animals were tested for epidermal sensitivity to the respective antigens. Three yielded positive results out of six experiments. Passive transfer of the sensitivity was not possible by intradermal injections of the exudate in guinea pigs. Passive transfer also failed in man when blood or lymph node extracts of sensitive patients were injected intradermally in a normal person.

In rabbits sympathectomy of the nerves leading to one ear of the rabbit increased both the allergic and the simple inflammatory reaction in that ear. High altitude does not seem to prevent sensitization in guinea pigs when neoarsphenamine (Neosalvarsan) is used as the sensitizer. High altitude exerted an inhibiting influence on the reaction of intradermal nature. Guy has been able to show that guinea pigs may be made more sensitive to contactants by disturbing their normal sleep cycles and by other neurogenic factors.

Systemically administered cortisone decreased the skin reactions caused by primary irritants such as croton oil and the hypersensitivity reaction to 2,4-dinitrochlorobenzene in guinea pigs. The appearance of the skin reactions was delayed in both types of reaction. Sensitization could not be prevented by systemic administration of cortisone. Adrenalectomized guinea pigs showed enhanced cutaneous reactivity as evidenced by shorter latent periods and by skin reactions to lower concentrations of test substance. Similar results were not obtained in mice.

Guinea pigs were used to show the value of the antihistaminics against histamine which plays an active role in the development of the initial phase of the reaction to primary irritants as well as in the production of contact dermatitis. Experimentally, tripelennamine (Pyribenzamine) apparently helped to prevent severe contact dermatitis, and also a primary irritant counteraction was enlisted.

A method in which a known dosage of a test substance is applied uniformly over an area of skin the size of which is accurately controlled was devised. Humans had considerable variation in the length of the period before reactions appeared. Guinea pigs were more regular.

R. L. Mayer found that many aromatic amines and dyes which were strong skin sensitizers also produced atypical epithelial proliferation or cancer.

ANAPHYLAXIS IN ANIMALS

Guinea pigs were sensitized anaphylactically to commercial solution of penicillin by a single intradermal injection and to crystalline sodium penicillin by a single intradermal or by four daily intraperitoneal injections. Anaphylactic sensitization to penicillin G may be induced by infection of the skin with Trichophyton gypseum in guinea pigs. Schultz-Dale tests showed a common antigen to penicillin and T. gypseum. Peck and Siegal, on the other hand, conclude from their guinea-pig experiments that the antigen inducing penicillin sensitivity and the antigen inducing Trichophyton sensitivity are different and do not cross react.

Penicillin has increased toxicity for the guinea pig, 250 units in a single injection resulted in death in a high percentage of animals. Studies have been made on the efficacy of the ethylenediamine drugs, tripelennamine pyrilamine (Neo-antergan) maleate, Antergan (dimethylaminoethylbenzylaniline) and diphenhydramine (Benadryl) in preventing fatal histamine shock in guinea pigs. Intracutaneous injection of

old arsphenamine sensitizes the skin to both arsphenamine and neoarsphenamine but with old arsphenamine only an intravenous injection produces anaphylaxis in guinea pigs.

By conventional methods of testing in the rabbit for Shwartzman potency no Shwartzman active principle could be demonstrated in penicillin, dehydrostreptomycin sulfate, chlortetracycline (Aureomycin), chloramphenicol (Chloromycetin), or oxytetracycline (Terramycin).

The syndrome of anaphylaxis in guinea pigs is unaffected by pretreatment with histaminase. Intracutaneous wheals produced by histamine in normal as well as in allergic persons are not altered by oral pretreatment with histaminase.

Nelson, working with mice, has been able to prevent anaphylaxis to horse serum by using small amounts of cortisone. Studies of the electrolyte changes occurring during anaphylaxis revealed a rise in sodium and chloride ions in the tissue of the hind leg and a loss of potassium ion.

Guinea pigs were used in a state of severe vitamin C deficiency, and the anaphylactic shock produced by horse serum was much less severe than in moderate hypovitaminosis C. Prolonged administration of unsaturated oils to guinea pigs which had been sensitized to horse serum did not prevent anaphylaxis following injection of horse serum. Guinea pigs receiving cortisone daily for seven months and then actively sensitized with horse serum died in severe anaphylactic shock after intrajugular injection of the shocking dose of serum.

By intravenous injection of sorbitol monolaurate, urticaria was produced in dogs, and this method supplies a useful method for studying antiurticarogenic agents.

NUTRITION

When a diet low in vitamin A and vitamin D was fed to rats, follicular hyperkeratosis leading to formation of keratotic plugs in the hair follicles resulted. In addition, sebaceous glands and dermal fat stores atrophied, but these changes were not considered specific sequalae of vitamin A deficiency.

Black and piebald rats maintained on a vitamin-B-complex-free diet supplemented with thiamine, riboflavin, nicotinic acid, pyridoxine, and choline developed graying of fur in three to seven weeks, with retardation simultaneously in growth and appearance of coarse fur, inflammation of the nose, blood-caked whiskers, and adrenal hemorrhages. One hundred micrograms of calcium pantothenate daily prevented development of the achromotrichia and restored black pigmentation in four to six weeks in the fur of the rat. Administration of adrenocortical extract, desoxycorticosterone acetate, thyroid, and anterior pituitary extract failed to prevent the graying of the fur or the recurrence of adrenal hemorrhages in rats on diets deficient in pantothenic acid. In rats cystine when added in amounts of 1 to 2% to the diet delayed the development of alopecia due to chronic thallotoxicosis and increased the survival period of animals by many weeks. Two per cent dl-methionine was less effective. Graying of black rats due to thallium was not prevented by pantothenic acid, but was reduced by 2% cystine.

The antiacrodynic potency of a substance was tested by treating it as a supplement of a diet producing rat acrodynia. This potency is present in the unsaturated

fatty acids and has no relationship to vitamin C or D. Pyridoxine (vitamin B_6) was curative in rat acrodynia only if the animals were maintained on curative doses of essential fatty acids.

Sullivan and co-workers have presented an interesting series of experiments on nutrition of the rat. Rats fed an experimental ration including uncooked egg white, developed a severe pruritic exfoliative dermatitis which was corrected readily by biotin extracts. Vitamin B deficiency produced thin atrophic skin, while removal of vitamin A from the diet resulted in generalized cutaneous lesions of small squamous plaques.

Vitamin B2(G)-deficient Wistar strain of rats developed "dyssebacia" with atrophy of the sebaceous glands of the tail; this was cured by combination of vitamin B_6 and riboflavin. Pellagra patients also developed dyssebacia with hypertrophy of the sebaceous glands and were cured by autoclaved yeast or crude liver extracts. There were no differences in the local cutaneous response to infection on the part of the five groups of white rats fed diets containing different amounts of fat. Higher lymphocytosis was seen with high-fat diet in response to cutaneous infection.

METABOLISM

The Warburg apparatus was used on excised human and rat skin to measure respiration. It was found that lotions and creams depressed the respiration. The consumption of oxygen, water, phospholipid, and the total lipid content of the skin of normal albino rats declined with age to a relatively constant value.

Pillsbury and Kulchar found that the normal and the inflamed skin of a rabbit receiving normal diet did not vary in dextrose content. Water concentration of the inflamed skin of the rabbit was only slightly higher than that of normal skin. Dextrose content of the inflamed skin after injections of dextrose commonly varies from that of normal in that it is higher. The dextrose content of the epidermis and that of the whole skin coincided. Inflammatory crust had high dextrose content due to the drying of the exudate. Infection of the irritated skin developed more commonly in rabbits with dextrose than those on a normal diet. Dextrose value of the skin was always related to the content of the amount in the blood of the particular animal. Values for blood were always greater than for the skin. High carbohydrate intake made the course of an experimental infection on the skin severer in dogs. Diabetic (alloxan) rabbits did not have itching after injections of acetone, acetoacetic acid, or cholesterol. High dosages of glucose did cause itching. Ammonium chloride also caused pruritus. Milbradt found that characteristic disturbances of carbohydrate metabolism with a tendency to increase fasting blood sugar in rabbits and guinea pigs occurred with extensive dermatitis of chemical or mechanical origin.

Rabbits were fed lanolin diet, cholesterol-high diet for a considerable time. It was soon noted that liver damage, either by arsphenamine poisoning or intensive x-ray irradiation, tended to promote the formation of xanthomas. Also, it was noted that if the lanolin was continued over a long period of time severe liver damage would develop also.

The effect of vesicant agents on the metabolism was studied biochemically, with use of human and rat skin. The sulfhydryl enzymes were inhibited, and oxygen uptake was lowered. Dimercaprol reverses these changes.

No perceptible change in the skin irritability of dogs as a result of hypercalcemia was demonstrated.

Deficiency in magnesium content of the skin of neurodermatitis patients by histologic, spectrographic, and microincineration studies was demonstrated. An induced magnesium deficiency in albino rats was accompanied by dermatitis, general calcification of the tissues, and parathyroid enlargement. Other workers found the two conditions not similar.

Hechter reported that experiments indicated that the spreading produced by hyaluronidase not only was dependent on enzyme concentration but was directly related to an increase in interstitial pressure produced by fluid injected in performing the test. Methemoglobin was used as an indicator on abdominal skin of rabbits. The spreading effect of hyaluronidase in rabbit skin was not altered by x-ray therapy as long as six weeks after treatment.

INFECTIONS

(*a*) *Fungus.*—Trichophyton gypseum infection spread to normal guinea pigs by contact with infected animals. DeLamater and Benham studied experimental infections with dermatophytes in guinea pigs, rabbits, and cats. They found that the hypersensitivity to Trichophyton was developed only during the course of an infection. It rose gradually during the infection and reached its peak in two to three weeks after the lesions were healed. This hypersensitivity gradually decreased over a period of months after the infection. Immunity to reinfection was established concurrently with the allergy during the course of the infection and appeared to be closely associated with it. This immunity gradually declined and lost its protective ability after a period of some months. Local complete immunity associated with a diminished allergy was demonstrated in the lesion sites. Minimal allergic response developed in animals of young age (newborn); also, this may explain their greater susceptibility to progressive ringworm infections than older animals.

Wharton, Reiss, and Wharton found that rabbits could be immunized to Trichophyton purpureum by emulsified fungus and showed a marked lymphocytosis in contrast to those that were susceptible to infection. Precipitating antibodies were detected in the immunized rabbits and in some of the infected animals. This antigen may be of therapeutic value. Topical applications of methyltestosterone and estradiol U. S. P. in ointment form were curative for experimental T. purpureum infections in castrated rabbits. When given the hormone by injection, the animal failed to improve. A chronic T. purpureum was produced in eight castrated male rabbits. One year later, twice weekly intravenous injections of heavy force suspension of the fungus were begun. Six months later the animals were killed and examined for evidence of vascular damage. No damage was found. Repeated injections of Trichophyton did not alternate the course of experimental infections with T. purpureum in castrated rabbits. In guinea pigs experimentally infected with Achorion quickeanum treatment with cortisone prolonged the course of the infection but corticotropin (ACTH) did not do this. The trichophytin reaction was not influenced.

Mice were inoculated intraperitoneally with three strains of T. purpureum (rubrum). Adaptation of the fungus to deep-tissue environment challenges the present classification of this organism as an obligatory superficial parasite.

Trichophytin stimulates the production of complement-fixing antibodies and precipitins when injected into rabbits. It is suitable as an antigen in antigen-antibody reactions. Guinea pig sera has fungistatic power. Ascitic fluid was found to be only moderately fungistatic. Mice and rabbits were used to various fungistatic agents.

Arthritis in rabbits was produced by injection of Monosporium apiosperum cultures into the joint spaces. Experimental blastomycosis has been produced in mice, guinea pigs, and monkeys. This allows for better testing of various chemotherapeutic agents.

Guinea pigs infected with Blastomyces dermatides develop a sensitivity to the organism; the polysaccharide part of the organism has been thought to be responsible.

Experimental histoplasmosis in the rabbit produced manifestations of adult nodular ulcerative cutaneous lesions.

Paracoccidioides brasiliensis is not pathogenic for mice, guinea pigs, rabbits, cats, or dogs, but only for the rat. Even the rat is indifferently affected. The Coccidoides immitis is highly virulent for rats, mice, guinea pigs, and cats.

Histoplasmin was found to be nontoxic to guinea pigs and mice. It did not produce irritation or sensitization on repeated intradermal injections to guinea pigs. In laboratory animals infected experimentally with Histoplasma, intradermal testing with 0.10 cc. of a 1 : 100 dilution of the extract generally produced definite skin reaction. Cross reaction with coccidiodin and blastomycin in the animal were numerous. Also, in a group of 69 mental patients with chronic lung lesions, 25% reacted to both histoplasmin and blastomycin.

(*b*) *Syphilis.*—In rabbits inoculation into testicles immediately results in spirochetemia. Heat applied to the testicles of rabbits prevented the development of syphilitic testicles. Spontaneous spirochetosis in the rabbit was due to Treponema cuniculi. This organism is identical with Treponema pallida. Therefore one may see changes in normal rabbits identical with those due to syphilis in the viscera of rabbits. Results of antisyphilitic therapy must be checked. In rabbits congenital syphilis was not produced.

Virulent T. pallida were present in the vagina in secondary, relapsing syphilis as well as in menstrual blood proved by animal inoculation. Infectiousness through the vagina was periodically recurrent. Saliva obtained from the parotid ducts of seven patients with florid secondary syphilis was inoculated into rabbits, with negative results.

Rabbits were injected with flocculate obtained from the serum of cases of human syphilis and this flocculate seemed to be antigenic, as 10 times as much flocculate was obtained as was previously injected. Rabbits were given dead T. pallida with suitable controls; subsequent inoculations yielded equally positive results in both groups.

Klauder has tried to uncover the cause of interstitial keratitis experimentally, without success.

House mice have been infected with T. pallida, and in white mice the spirochetes penetrated the central nervous system; this did not occur in rabbits. An asymptomatic infection results in mice, which was easily transferred to rabbits by brain suspension; the results indicated definite neurotropism.

Rosahn found that the longevity in mice as well as in human beings was adversely affected by syphilitic infection, but death was not usually the direct consequence of the disease.

Osborne and co-workers have reported a microscopic technique for demonstrating arsenic trisulfide in tissues occurring after the use of various arsenicals.

Acetarsone had little effect in experimental trypanosomiasis. It is worth while in experimental rabbit syphilis. Maximum tolerated dose of oxophenarsine hydrochloride (Mapharsen) for rabbits with the continuous intravenous drip method of administration was about 0.012 gm. per kilogram of weight once a day for five days in succession, totaling 0.06 gm. per kilogram. With syringe method the single maximum tolerated dose was about 0.015 gm. per kilogram. Seven rabbits given massive arsenotherapy by bone-marrow-infusion drip each day for five successive days resulted in five of the rabbits having pulmonary emboli.

A solution of sodium dehydrocholate added to a solution of neoarsphenamine before injection greatly increased the ratio of the weight of the liver to the percentage of neoarsphenamine retained, the "ratio of protection." One hundred twenty-three rabbits poisoned with mercury arsenic failed to show any protective action from sodium thiosulfate and sodium *p*-sulfhydril phenyl sulfonate. The protective effect against arsphenamine (arsenobenzol) exerted on the liver by liver extract in rabbits seemed to be due to a binding or immobilization of the glycogen in the liver cells.

Various studies have been carried out to study the efficacy of bismuth compounds in experimental syphilis. Bismuth was found in the brains of only 2 out of 12 rabbits studied after therapy. Bismuth arsphenamine sulfonate (Bismarsen) was probably as effective as arsphenamine in experimental rabbit syphilis. Three groups of rabbits were injected with various amounts of bismuth. The kidneys were found to have the higher concentration of bismuth, and the liver contained a large amount of the metal. There was an increase in the number of polymorphonuclears and lymphocytes. Pathologic changes were found in the muscles, kidneys, and heart; there were considerable necrosis and chemical abscesses in the muscles at the site of injection.

Kolmer has studied the efficacy of penicillin by various doses in saline solution vehicle and peanut-oil-beeswax vehicle and found that the single minimum curative dose of penicillin in the former vehicle was more than 100,000 units per kilogram of weight, while with the latter vehicle 10,000 units per kilogram was the single curative dose. He has found a synergistic effect with oxophenarsine hydrochloride, bismuth and potassium tartrate, and bismuth subsalicylate. Bismuth penicillin suspended in sesame oil with 2% aluminum monostearate was approximately twice as curative as sodium penicillin suspended in peanut oil and white wax in the treatment of acute syphilitic orchitis in rabbits. Over a 10-day period 450,000 to 600,000 units per kilogram (total dose) was the minimal curative dose by oral route in rabbit syphilis.

Magnuson produced asymptomatic neurosyphilis in white mice by intraperitoneal injection of 10^6 Treponema pallida (Nichols) three months prior to treatment. A total dose of 14,000 units of penicillin per kilogram in four days cured 50% of the animals, while a total dose of 64,000 units per kilogram cured 90%.

Nelson's studies on the treponemal immobilization test have depended on spirochetes from rabbit syphilis.

(*c*) *Virus.*—Rabbits have long been important in the isolation of herpes virus through the corneal scarification test. Human strains have also been adapted to mice. Rabbits and guinea pigs have been used in the neutralization test.

The passage of lymphogranuloma venereum virus through mice by intracerebral inoculation produced a good source for the Frei antigen. There is cross immunity in mice between meningopneumonitis virus, but there is no definite cross immunity between lymphogranuloma and psittacosis.

Desensitization of guinea pigs previously infected with vaccinia virus did not result in a loss of immunity. This seemed to indicate that hypersensitivity and immunity may be dissociated experimentally.

Many attempts to isolate virus agents from patients suffering from pemphigus and dermatitis herpetiformis have not been productive of consistent results. Mice injected intracerebrally with serum or blister fluid from patients with bullous diseases showed no clinical signs; electrophoretic blood serum protein studies on mice injected showed no changes compatible with the patterns occurring in persons with the bullous disease. No agent was transmissible.

(*d*) *Tuberculosis.*—In the white rat tuberculosis-like lesions did not occur in response to intracutaneous injection of virulent forms of mycobacteria, Escherichia coli, or silicon dioxide. Localized noncaseating epitheloid lesions occur after intracutaneous injection of Mycobacterium tuberculosis hominis and avium of standard virulence. Infective bacteria appear to remain localized, and when lesions occur the tissue changes show a tendency to undergo resolution. All the reactions between the organism in the tuberculosis infections were slower in the rabbit than in the guinea pig. Probably indifference to tuberculous principle on the part of the rabbit organism explains this. This is inborn and not acquired through refractory substances. Intracutaneous injection of living and dead tubercle bacilli always leads to production of changes in young cats which are fundamentally different from lesions described early in the guinea pig and rabbits. A diffuse suppurative tissue infiltration occurs in the upper layers of the skin, with a deep nodular infiltrate in the subcutaneous layer. Reinfection with tubercle bacilli produces the same tissue reaction as the first inoculation to a noninfected cat. A guinea pig has a different capacity to react. The guinea pig belongs to that group of animals which as a result of the symbosis with the tubercle bacillus has obtained a high degree of adaptation. Man probably belongs to the same group.

In the guinea pig studies with repeated injections of tubercle bacilli showed the first reaction slightly less in the immediate vicinity of the primary inoculation and at a considerable distance from it, indicating that the tissues around the primary zone were less allergic than elsewhere.

Vitamin D administered orally to rabbits, mice, and cats in amounts exceeding tolerance doses produced progressive weight loss usually associated with heterotypic calcification.

(*e*) *Other Infections.*—Klauder and Rule have found that Erysipelothrix rhusiopathiae infection in mice responded to penicillin but not to streptomycin. Sulfanilamide alone is not too effective, but with penicillin a synergistic effect was obtained.

Rabbits showed cutaneous and subcutaneous hemorrhages after intravenous injection of a Streptococcus of the viridans group isolated from the nasopharynx of psoriatics, lichen planus patients, and urticaria patients.

No serologic specificity was demonstrable. Specific streptococci were isolated from pemphigus patients; these organisms were serologically identical. On intradermal injection of the dead organisms, bullae were produced in pemphigus patients. Five animals—mice, rats, guinea pigs, rabbits, and monkeys—were used, and the organisms were virulent. Sera from patients with pemphigus cut down on the motility of the organisms and were of differential aid in erythema multiforme, lupus erythematosus, and dermatitis herpetiformis, according to Welsh.

Hopkins and co-workers by intradermal injection of staphylococci produced in sensitized rabbits thickening of the epidermis, down growth of hair follicles, activation of hair growth, and encasement of the leucocytic mass by epithelium derived from the hair follicles. In addition, small horn cysts and follicular plugs resembling comedones frequently developed. Staphylococci allergy is probably not the only mechanism by which this picture can be induced. The cyst formation seems to be a defense mechanism similar to the formation of acne cysts.

Hecht, Sulzberger, and Weil showed that injection of rabbit skin antigen and Staphylococcus toxin resulted in formation of antibodies precipitating to homologous skin. Homologous skin alone was injected; antibody formation was questionable, or at most slight. Injection of Staphylococcus toxin alone resulted in formation of antibodies specific for toxin, not reacting with broth used to manufacture this toxin. The skin antigen used as well as the skin autolysates used for the precipitin reaction could not be made sterile. It is possible that the reaction might have been due to contaminating micro-organisms and their antibodies.

MISCELLANEOUS

Ears of rabbits were used to study the sclerosing effect of invert sugar and sodium morrhuate; results by macroscopic photography indicated that invert sugar was a better agent.

Venous obstruction for a 30-minute period resulted in a rise in interstitial pressure in the skin of mice from original levels of 2.6 to 4.6 cm. of water to a maximum of 33 cm.

Neither intradermal nor intramuscular injections of gold sodium thiosulfate solution produced chrysiasis in guinea pigs or rabbits when concurrent ultraviolet radiation was administered.

Local sweat response to intradermally injected acetylcholine has been studied in cats. The axon reflex has been studied in cats with similar findings in humans by Rothman and Coon.

Changes occurred in a guinea pig after inoculation of the material from a case of porokeratosis Mibelli which were similar or suggestive of porokeratosis pathologically.

In rabbits, 300 to 400 r are necessary to produce a suppression of spermatogenesis, 600 to 650 r are necessary to produce a temporary arrest in spermatogenesis, and 950 to 1,550 r are required to produce a permanent arrest of spermatogenesis. Two patients with carcinoma of the prostate were subjected to 300, 600, and 900 r and later subjected to orchidectomy without apparent arrest of spermatogenesis.

Increased capillary permeability in the skin following irradiation was demonstrated in the rabbits by use of trypan blue injected intravenously.

Neither local nor total body radiation affected in the rabbit the splanchnic removal of bacteria.

A study of the effect of thallium acetate on thyroidectomized albino rats in controlled experiments seemed to show that the thyroid gland does not play an important role.

Studies of undecylenic acid by oral route indicate that in a 2.5% ration it has marked inhibitory effect on the growth of rats.

COMMENT

Hopkins in his presidential address in 1948 gave a scholarly discussion of his ideas on measurement of the skin and the future of dermatologic development in the research sphere. He quoted Alan Gregg's statement, "Research is the response to curiosity, not to need." If this definition is used, many of these contributions which we have briefly gone over would not fit into research. However, most if not all of these efforts have been to measure accurately and eliminate guesswork and conjecture.

These reports here summarized have not dealt with contributions of basic sciences through which our ultimate goal of understanding diseases of the skin will be reached. But these contributions, in many ways, have enlightened the everyday routine of dermatology and its practice. The pathogenesis of many diseases or syndromes remains in the realm of the unknown, but stepping stones of understanding are unearthed through individual endeavor, regardless of magnitude. All attempts to clarify the whys and wherefores are worth while, even when the results are not of a positive nature. Small animal investigation, in spite of many difficulties in producing conditions similar to those encountered in humans and in interpreting results of animal experiments to human application, will continue to be a fruitful line of endeavor in furthering our knowledge. The more accurate the measurement the more gratifying is the outcome in clinical application, and in small animal research the same is true.

ABSTRACT OF DISCUSSION

Dr. Marion B. Sulzberger, New York: Dr. Callaway has done us all a great service by going through this careful and very painstaking compilation of the work done on small animals in dermatology. I am sure that we shall profit greatly when we are able to read his paper in toto.

The thesis that much has been learned, much is being learned, and much will be learned through animal experimentation on the skin needs no support before this audience. If we could not experiment on animals we would be obliged either to give up many opportunities for scientific progress and advances towards the mastery of human skin diseases or to subject human beings to painful and even dangerous experiments. Nevertheless, as Dr. Callaway and others have so rightly emphasized, there are tremendous differences between one animal species and another. There are therefore a great many gaps when one is trying to transfer results found in one species to problems dealing with another species; and we, of course, are still primarily interested in man and man's skin.

You know that certain compounds (I believe that thiouracil is one such compound) have a dramatically opposite effect upon thyroid function in rats as contrasted with mice, closely related as those two rodents are. I think that perhaps one of the nicest modern examples of the great difficulty in transferring, without proper correction, the results found in one species to another is the example of penicillin. When Fleming discovered penicillin, you know that he tested it for toxicity upon the leucocytes, upon the human white cells, before it was administered to man. If, as might well have been the case, Fleming had tested penicillin in the guinea pig, he would probably have come to the conclusion—just as Miescher and his co-workers and Peck and his co-workers did—that this material was primarily exceedingly toxic for animals, for mammals.

In other words, the doses, weight for weight, necessary to be therapeutically effective, killed guinea pigs when administered (not by sensitization, but in some primarily toxic way). With this result, penicillin might well have been withheld from human use.

One could multiply such examples, showing the tremendous differences to be expected when one is doing animal experiments.

In the field of sensitization, of course, that is particularly true. If you try to sensitize the skin of a guinea pig and you do succeed in sensitizing it with a simple chemical, let's say poison ivy, catechol, or dinitrochlorobenzene, you may get a degree of sensitivity which is tenfold of fivefold, perhaps sometimes as high as fifteen- or twentyfold, as great as it was originally; in other words, the primary irritating concentration will be only 5 times as great as the concentration, or 10 times as great as the concentration which elicits a reaction in the sensitized laboratory animal; whereas in human beings the potentiation can be as much as 1:100,000, 1:500,000, or 1:1,000,000 in the case of such things as poison ivy. Again, there is the difference in capacity for vesiculation, which you have heard discussed in comparing the animal skin and the human skin.

I should like to stop at this point and go on to what Dr. Callaway has suggested that we discuss, namely, to mention just a few of the future uses of animal experimentation. You know perfectly well that under certain conditions one simply cannot use man because of the dangers or impractability of the experimentation. We as dermatologists are most fortunately situated in that we probably can do more clinical experimentation on the organ which interests us, the skin, than can scientists in most other fields of medicine—because we have such a large organ to study, so much of it is available, and it is so easily accessible. Nevertheless, certain situations exist in which the animal experiment will be necessary and will bring us forward, where we could not get forward by doing direct human experiments. One of these, for example, is in the field of fungous infections.

Just now we are engaged, under a grant from the United States Army, in trying to study fungous infections in small laboratory animals. The idea was that although there are fungous infections available aplenty in man, superficial fungous infections by dermatophytes, nevertheless the assay of therapeutic materials is tremendously difficult. For instance, ordinary athlete's foot (which concerns the Army greatly still) is so erratic in its course and yields so readily (although often only temporarily) to many simple agents that it is very difficult to evaluate therapeutic measures on that object; so that we are confined, for instance, in our studies of new antifungal agents in man, to such things as Microsporum infections of the scalp of children or Trichophyton tonsurans infections of the scalp or Trichophyton rubrum infections of the skin and nails.

In studying the scalp infections and the nail infections caused by these fungi, it becomes apparent that it is the new-forming tissues which becomes infected. As has been pointed out recently by Kligman and others, the problem would seem to be what prevents new hairs from getting infected or new nails from getting infected. Something must happen, for instance, at puberty in Microsporum audouini infections, when the natural defluvium of the infected hair takes place and the new hairs have all acquired a resistance to new infection by the Microsporum fungus which is present.

In the attempt to study these factors, laboratory animals will certainly prove most useful, and we thought of the idea of using the infections of young puppies or kittens, and of young rabbits with Microsporum canis because there we can hope to produce an infection which is sufficiently aphlegmatic, sufficiently noninflammatory, and sufficiently lasting to parallel closely what one sees in M. audouini infections or T. rubrum infections in man.

Dr. Reiss and Miss Caroline and others of our group have just now succeeded in producing such infections in puppies, kittens, and young rabbits. These seem to be carrying out our expectations of a long-lasting, noninflammatory infection of hair and skin, in which we may be able to study systemic effects and new antifungal systemic measures which may prevent the new hairs from becoming infected. Such systemic therapeutic assays of new agents could never be permitted or be feasible in children or in adults affected by superficial mycoses.

Dr. Adolph Rostenberg, Jr., Chicago: As a newly initiated member, I feel somewhat diffident in getting up here, but inasmuch as Dr. Callaway's paper is concerned with animal research and that is an area in which I am extensively engaged, I could not help but comment on it.

I should first like to make a few remarks about certain difficulties inherent in animal research. As has been pointed out by both Dr. Callaway and Dr. Sulzberger, there are great differences between species. Even in the same species, there may be profound biochemical differences. A well-known example is found in dogs. The Dalmatian dog differs in its uric acid metabolism from all other dog races, and if one were studying something as profound and fundamental as uric acid metabolism and were not aware of this, one might go astray by using the wrong kind of dog.

A point that does not come up too often, but is worth mentioning is that if one goes outside the conventional laboratory animals, one must be careful about proper identification. To give an example, we were interested in the development of eczematous sensitizations in various species, and as some ferrets were available we thought we would endeavor to develop an eczematous sensitization in them. After we had finished with them, we had no particular use for the ferrets, but we saw no sense in just killing them. Maybe somebody could do something with them. Knowing a woman who runs a zoo in Chicago, we said, "Do you want some ferrets." She said, "Fine," so she came around. She thanked us very much and said, "But they're not ferrets." They happened to be the North American ferret, which is actually quite a different animal from the European ferret.

It is of some importance in labeling the animal to give its correct zoological name, because there is no reason to believe that you will get the same results with the ferret we used, Putorius putorius, as a European worker might with some other ferret. Similar remarks apply to the hamster. The name "hamster," is not adequate. There are at least three distinct genera among that animal, so one has to be sure in which genus the animal is—and, incidentally, the identification may be difficult.

Another point I should like to make concerns genetic differences between members of the same species. It is well recognized that when one tries to sensitize, for example, the guinea pig, different strains will respond quite differently. We have strains of guinea pigs that are utterly worthless from the point of view of developing an eczematous sensitization. One just cannot sensitize them, even with potent sensitizers such as 2:4 dinitrochlorobenzene. With other strains of guinea pigs, one can sensitize roughly 90% by the same technique. Of course, in evaluating results a factor of obvious importance is whether one was dealing with a homozygous or heterozygous strain of animals. Homozygous strains are essential in order to have reproducible results, and comparability between the results of one laboratory and another. There is little point in comparing sensitization results when one laboratory is using a strain that does not sensitize and another is working with a strain that is easily sensitized.

The importance of genetic factors not only applies to sensitization phenomena but also applies to the genesis of many infections. An indication of this is given by some of the work that has been done on the genetic aspects of human tuberculosis, in comparing the incidence of tuberculosis in identical and fraternal twins. In the case of identical twins, roughly, when one twin came down with tuberculosis, 85% of the twin mates came down; whereas in fraternal only 25% came down. Now, in both kinds there is, approximately, the same environment, so that the differences could be ascribed only to the varying genetic make-ups.

In conclusion, I suppose we might sum up the role of animal research in the words of Alexander Pope, that "the proper study of man is man," but the animal is often an indispensable adjunct for this.

DR. MAURICE SULLIVAN, Baltimore: The ultimate test animal for therapeutic experiments is man. However, it is almost always necessary to conduct extensive tests in animals before definitive human experiments can be undertaken. In investigative dermatology it is essential to employ mice, rats, guinea pigs, cats, dogs, swine, and monkeys to obtain information that finally relieves human suffering and saves life. Many illustrations come to mind. I shall mention only a few. We are presently engaged in a project for the Surgeon General's Office to find improved fungicides for systemic and localized infections, and we are obliged to test thousands of remedies. It is not possible to find enough patients, for example, with systemic Candida albicans infection to test all the drugs which show promise. Therefore, we must use the mouse, an excellent animal for this purpose. It would seem that there should be enough patients in our large clinics and military installations to serve as test subjects for topical remedies to combat superficial fungus infections. In spite of the widespread incidence of dermatophytosis, we must use animals to obtain certain adjunctive information regarding the action of fungicidal drugs. Also, it is essential

to study fungus diseases in such hosts as dogs, cats, and cattle to secure vital information not obtainable from human experimentation. Although much of our research on nutritional dermatosis in rats was not applicable to clinical dermatology, there were important contributions to the science of nutrition which account for the better state of health of our sons and daughters. Who among us has an offspring of smaller stature than his parents? The physical welfare of our younger population may in great measure be attributed to the research with rats. Such benefit to human happiness could not have been secured from human experimentation alone. Swine are invaluable in dermatologic research because of the similarity of their hides to human skin. At present, we are conducting experiments on primary irritation effects, and the results of our experiments should have wide clinical implications which may prove of benefit to countless men. Although Dr. Sulzberger has emphasized that the skin of man is an easily accessible and large test organ, it is not possible to perform experiments on human beings similar to those that can be performed with swine. I refer to such procedures as one in which multiple applications are made to swine skin, and the animals are killed at periods of one, two, three, four, and five hours, etc., to obtain material for the study of reaction patterns. Obviously such experiments cannot be performed in human beings, and the information from such experiments is transferable to humans. Analysis of the species differences referred to by Drs. Sulzberger and Rostenberg will be productive of valuable data on immunologic and allergic phenomena in skin diseases. For comprehensive understanding of the physiology of human skin there should be no limit to the pursuit of comparative studies with many different animals, which will provide opportunities to study functional patterns in similar tissue that varies anatomically in appendages and layers.

It would be a sorry day for the discipline of dermatology if laws were enacted which would in any measure prevent the use of animals for experimentation. Drs. Callaway and Hambrick are to be congratulated for compiling a chronicle of the important contributions of experimental animal research in our specialty.

DR. STEPHEN ROTHMAN, Chicago: Dr. Sulzberger's remarks about the pitfalls were partially apropos. The factor of hair is one of the most serious. I am sure that every investigator, when hair enters the picture, casts about for the most appropriate hairy animal, and, vice versa, when he wishes to avoid the factor of hair, he inquires for the appropriate hairless or nonhairy animal. On the face of it, it might appear that the Mexican hairless dog would be suitable, but it is "pesky" and vicious. Hairless rats can be bred only with difficulty, but the real obstacle here is that the hairlessness is not phylogenetic but a manifestation of disease. It is a secondary effect of thyroid deficiency. Therefore, one is not working with a normal animal.

With respect to sebaceous glands, one of the most cruel revelations we have had lately (Parnell, J. P.: Postnatal Development and Functional Histology of the Sebaceous Glands in the Rat, *Am. J. Anat.* **85**:41-72 [July] 1949) is the fact that the sebaceous cycle in our commonly employed mice varies over the course of the month, and if we base our observations on what the sebaceous glands show at, say, early in the cycle of the month, we will get entirely different results from those at the end of the cycle.

There is one point which has not been brought out this morning, and that is in respect to castration of animals. I think that it is not practiced sufficiently. I am sure, certainly in the studies of functional dermatoses, that running a parallel series of animals, that is, a series in which castration has been practiced, is important. This is the place where small animals have the big advantage in usefulness compared to experiments with man, I take it.

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LIFE HISTORY OF NAEVUS SYRINGADENOMATOSUS PAPILLIFERUS

HERMANN PINKUS, M.D.
MONROE, MICH.

IT IS THE purpose of this presentation to point out a sequence of events which appears to be typical in the development of naevus syringadenomatosus papilliferus, and by doing so to aid in the clinical recognition of this often unsuspected tumor. In addition, a clarification of some debated points in the histogenesis of naevus syringadenomatosus papilliferus will be attempted. The discussion will be restricted to those papilliferous growths which most commonly occur on or near the scalp and which develop in a preexisting lesion. Related tumors, particularly the papilliferous cystadenomas of the vulva, which Anderson [1] discussed before this Association three years ago, will not be considered.

Naevus syringadenomatosus papilliferus is judged a rare lesion by most authors. Biberstein (1926),[2] Reuterwall (1933),[3] and Sachs and Lewis (1937) [4] surveyed the older literature and collected approximately 40 cases. Probably an equal number has been added since that time, but no complete analysis of the literature is intended in this paper. Only two recent authors (Nödl,[5] Percival [6]) state that naevus syringadenomatosus papilliferus is fairly common. It is likely that a high rate of suspicion can increase the number of observed cases, particularly if there are included not only large and spectacular tumors, such as the one shown in Figure 1 (Case 2), but also hidden, almost microscopic lesions, which sometimes are found only by examination of serial sections in suspected cases.

PERSONAL CASES

One such case is illustrated in Figure 2 (Case 3). This was a small pedunculated papilloma near the anterior axillary fold in an elderly man. It was removed because it annoyed the bearer when it was rubbed by clothing and became irritated and moist. Sections cut through the center of the small tumor showed at one side of the base a funnel-shaped sinus into which several duct-like structures opened. These and the adjoining parts of the tumor were lined with high columnar epithelium, which rested on a second row of cuboidal cells. Serial sections of the remaining tissue showed that this was a fully developed though microscopic, syringadenoma papilliferum which was connected with some of the apocrine glands of the axilla.

Interest in the early stages of syringadenoma which had been aroused by this case in 1937 was strengthened by the following experience several years later.

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From the Detroit Institute of Cancer Research; the Department of Dermatology, Wayne University College of Medicine, and the Department of Pathology, Wayne County General Hospital, Eloise, Mich.

Fig. 1 (Case 2).—Clinical aspect of naevus syringadenomatosus papilliferus in the right temporoparietal region of the scalp of a 60-year-old woman.

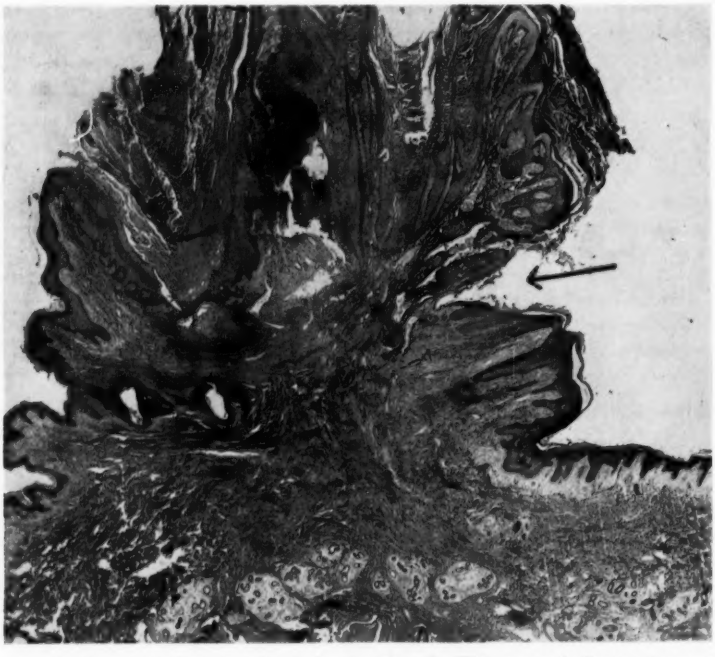

Fig. 2.—Section through the entire lesion in Case 3. The arrow indicates the opening of the papilliferous sinus. The atypical fibrous core of the small papilloma and the presence of apocrine glands complete the picture of naevus syringadenomatosus papilliferus. × 10; hematoxylin and eosin.

CASE 17.—In March, 1943, a 16-year-old boy asked for removal of a birth mark which bothered him by its unsightliness. On the back of the neck, overlying and parallel to the edge of the left trapezius muscle, were two patches composed of soft light-brown papules and papillomatous nodules. The lesions were dry, not markedly hyperkeratotic, and presented the clinical picture of a linear papillomatous nevus. The lateral and shorter one of the two linear plaques was excised through the full thickness of the skin, and the wound was closed with sutures. The site healed satisfactorily except for slight temporary thickening of the scar. Histologic examination showed hyperpigmented papillomatous structures without nevus cells and without obvious abnormalities of the appendages. Thereupon, the remaining larger part of the nevus was destroyed by electrocautery. The denuded area epithelized within a few weeks, but four

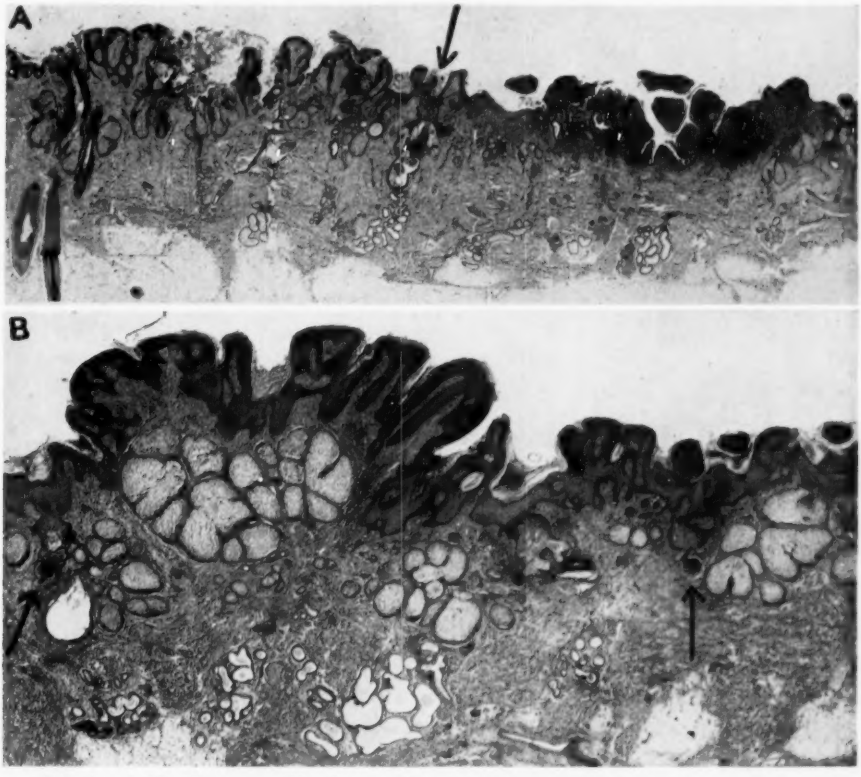

Fig. 3.—*A* (Dr. Eugene A. Hand's case, Case 15), naevus syringadenomatosus papilliferus in an 18-year-old girl, showing the cystadenomatous portion on the right and the "preadenomatous" hamartoma on the left. Normal scalp, with normal pilary complexes, is at the far left. Basal-cell epithelioma had developed in another portion of the nevus. Mature dilated sweat glands of apocrine type are present in the nevus, and one of them (arrow) opens into a malformed pilosebaceous complex by means of a cystic duct showing early papilliferous changes. Note the dense plasma-cell infiltrate in the adenomatous portion. × 8; hematoxylin and eosin.

B (Case 19, surgical specimen supplied by Dr. Hardee Bethea), papillomatous and sebaceous nevus with dilated apocrine glands in a 28-year-old man. Malformed hair roots are seen in two places (arrows). The structure of the lesion is identical with that of others in which cystadenomatous portions were found, even to the presence of plasma-cell infiltrates in some places, but no papilliferous structures were encountered in multiple sections. × 28; hematoxylin and eosin.

months later fresh papules arose in the scar and became larger than the original ones had been. These papules were firm, pink, and crusted and exuded serosanguineous fluid from multiple

TABLE 1.—*Life History of Naevus Syringadenomatosus Papilliferus*

Case No.	Physician(s) Supplying Information and Bioptic Material	Age	Race	Sex	Age When Original Lesion Appeared	Nature of Original Lesion	Change When? In What Respect?	Trauma?	Size at Operation, Cm.	Location	Histological Diagnosis and Comment
						Group 1: Naevi Syringadenomatosi Papilliferi					
1	C. J. Courville, Morris Wilson	63	W	M	2 yr.	Bald infiltrated plaque	2 yr. previous bleeding, crusts	Picked at lesion	2 × 1.5	Right parietal near midline	Naevus syringadenomatosus papilliferus Malformed pilary complexes, apocrine glands
2	S. E. Gould, Hermann Pinkus	60	N	F	57 yr.?	Papillomatous plaque	1 yr. previous moist, exuberant proliferations	?	7 × 3	Right temporo-parietal	Naevus syringadenomatosus papilliferus Papilliferous cystadenoma (or low-grade adenocarcinoma) of nipple treated by amputation of breast 7 yr. previous
3	Hermann Pinkus	50	W	M	Many yr.	Pedunculated papilloma	Some months previous, became moist	Rubbed by clothing	1 × 1	Left anterior axillary fold	"Hidden" naevus syringadenomatosus papilliferus in guise of pedunculated papilloma
4	Leo Orecklin	50	W	M	Early childhood	Verrucous	Increased in size, became crusted during previous 2 yr.	No	2 × 2	Scalp, right frontal	Naevus syringadenomatosus papilliferus Hypertrophic sebaceous glands; apocrine glands
5	Stephan Epstein	45	W	M	Many yr.	Verrucous	Recently became moist	?	?	Scalp	Naevus syringadenomatosus papilliferus Malformed pilary complexes; atypical sweat glands
6	James R. Rogin	40	W	F	Birth	Bald verrucous plaque	1 yr. previous crusted, irritated; malignant change suspected	No	3.5 × 3.5	Central vertex	Naevus syringadenomatosus, eccrine-gland type
7	Milton Sorock	39	W	M	Birth	?	20 yr. previous recurred as gray moist papilloma	Tied off with string	1.2 × 1.2	Abdominal skin above umbilicus	Naevus syringadenomatosus papilliferus Recrudescent lesion; cystic deep apocrine glands; iron granules found in superficial adenomatous portion
8	C. J. Courville	36	W	F	6 yr.	Partly bald plaque studded with yellow papules	1 yr. previous, part became crusted, bled easily	Accidental injury with sharp object	3.8 × 3.8	Vertex	Naevus syringadenomatosus papilliferus Malformed pilary complexes, atypical sweat glands
9	James R. Rogin	33	W	M	18 yr.	Bald infiltrated plaque	Became verrucous, irritated, oozing	Comb	3 × 2	Vertex	Naevus syringadenomatosus papilliferus Small biopsy shows atypical sweat glands; no pilary complexes in specimen
10	William L. Poole	25	N	F	20 yr.	Infiltrated plaque	Became darker and thicker	No	3 × 3	Neck	Naevus syringadenomatosus, probably eccrine-gland type No pilary complexes in specimen
11	Leo Orecklin	24	W	M	Infancy	Verrucous plaque	1 yr. previous increase in size	Removed by desiccation at age 17	1.5 × 1	Right side of forehead	Naevus syringadenomatosus papilliferus Malformed pilary complexes; biopsy too superficial for evaluation of sweat glands
12	Hermann Pinkus	23	W	M	Birth	Bald scar-like area	1 yr. previous 2 keratotic papules developed (see text)	Comb	10 × 3	Right parietal frontal	"Hidden" naevus syringadenomatosus developing in a large organomatous nevus with preponderance of sebaceous glands; apocrine glands present
13	Kurt Wiener	22	W	M	Unknown	Verrucous	Recurred, formed pedunculated ulcerated tumor	Removed surgically at age 17	1 × 1	Medial to left eye	Naevus syringadenomatosus papilliferus Recrudescent lesion; biopsy material does not permit evaluation of pilary complexes and sweat glands
14	H. H. Holman, A. E. Schiller	18	W	F	Birth	Verrucous	2 mo. previous moist granulations developed	Small excrescence removed	?	Scalp	Naevus syringadenomatosus papilliferus Biopsy material does not permit evaluation of underlying structures
15	Eugene A. Hand	18	W	F	3 yr.	Verrucous	Some months previous papule developed	Comb?	3 × 3	Left parietal	Naevus syringadenomatosus papilliferus Greatly malformed pilary complexes with development of typical basal-cell epithelioma in one place; apocrine glands contain iron granules
16	I. Botvinick	16	W	M	Birth	Verrucous	1 yr. previous became inflamed, crusted	No	3.8 × 2.5	Scalp, parietal	Naevus syringadenomatosus papilliferus Malformed pilary complexes, apocrine glands

Case No.	Physician(s) Supplying Information and Bioptic Material	Age	Race	Sex	Age When Original Lesion Appeared	Nature of Original Lesion	Change When? In What Respect?	Trauma?	Size at Operation, Cm.	Location	Histological Diagnosis and Comment
17 (*b*)	Hermann Pinkus	16	W	M	Birth	Papillomatous linear nevus	Recurrence, moist (text)	Desiccated	5 × 1	Neck, over border of left trapezius muscle	Nævus syringadenomatosus papilliferus Recrudescent lesion involving apocrine glands and some eccrine glands
						Group 2: Organomatous Nevi Without Syringadenoma					
						A. Postadolescent and Adolescent Cases					
18	Alice E. Palmer	44	W	F	At least 20 yr.	Papular	Gradual enlargement to form linear plaque of yellow papules	?	3 × 0.5	Right post-auricular	Epidermal and sebaceous nevus with malformed pilary complexes; atypical sweat glands, underdeveloped
19	Hardee Bethea, Hermann Pinkus	28	W	M	Birth	Bald plaque	More verrucous after puberty; superimposed papule previous few months	Irritated by tight operating room cap	4 × 3	Right temporo-occipital	Organomatous nevus with malformed pilary complexes and cystic apocrine glands; iron granules found; lesion similar in all respects to Cases 5, 8, 12, and 15 except for lack of papilliferous duct
20	Hermann Pinkus	21	W	M	Birth	Linear plaque	Gradual increase in size	No	1.05 × 0.3	Right labio-mental region	Epidermal and sebaceous nevus with malformed pilary complexes and apocrine glands
21	Hermann Pinkus	17	W	M	Child-hood	Papillomatous plaque	No change	No	2.5 × 0.8	Suboccipital	Papillomatous epidermal nevus with malformed pilary complexes and apocrine glands; iron granules found
17 (*a*)	Hermann Pinkus	16	W	M	Birth	Papillomatous linear nevus	More papules formed	No	3 × 1	Left trapezius border	Papillomatous nevus with fairly normal pilary complexes Eccrine and apocrine glands present; iron granules found in latter
22	Hermann Pinkus	13	W	M	Birth	Papules forming linear plaque	6 mo. previous verrucous exerescence formed	No	1 × 0.2	Left side of nose	Organomatous, mostly sebaceous, nevus with few short apocrine glands
23	Hermann Pinkus	13	W	F	Birth	Brown macule	Recently became papillomatous with greasy hyperkeratosis	No	1.3 × 0.5	Left trapezius insertion near hairline	Papillomatous epidermal nevus with malformed pilary complexes and incompletely developed atypical (apocrine?) sweat glands
24	Thomas H. Miller	12	W	F	Birth	Bald spot	2-3 mo. previous began to grow, became elevated, velvety	No	1.5 × 1.5	Right parietal	Papillomatous epidermal nevus with malformed pilary complexes and some apocrine glands
25	I. Botvinick, L. W. Gardner	10	W	F	Birth	Bald, somewhat pigmented plaque	Gradual extension and development of 2 new papules	No	2.5 × 2.5	Left occipito-temporo-parietal	Papillomatous epidermal nevus with hypertrophic sebaceous glands and well-developed apocrine glands; hairs deformed
						B. Preadolescent Cases					
26	Hermann Pinkus	12	W	F	Child-hood	Pigmented papules forming a plaque	Gradual enlargement	No	1 × 1	Right scapular region	Papillomatous epidermal nevus with large sebaceous glands Atypical, probably eccrine sweat glands
27	Owen S. Hendren	11	W	M	Birth	Smooth yellowish plaque	2-3 mo. previous became verrucous	Has been very pruritic	3 × 3	Scalp	Papillomatous nevus with malformed pilary complexes and groups of nevus cells; biopsy too superficial to determine status of sweat glands
28	R. J. Fink	10	W	F	Early life	Brown granular elevated bald area	Recently became more extensive	No	3.8 × 1.8	Scalp	Papillomatous epidermal and sebaceous nevus; possibly some not fully developed apocrine glands
29	Thomas H. Miller	9	W	F	Birth	Smooth bald patch	Recent increase in size, became elevated, rough	No	2 × 1	Vertex	Papillomatous epidermal nevus with malformed pilary complexes No sweat glands present in biopsy
30	Hermann Pinkus	6	W	M	Birth	Papillomatous plaque	Gradually became more prominent	No	5 × 0.5	Suboccipital	Papillomatous epidermal nevus with malformed pilary complexes and atypical sweat glands
						Group 3: Tumor of Nonhairy Skin					
31	William L. Poole	55	N	M	45 yr.	Verrucous	Within previous 2 mo. formed pedunculated papillomatous mass	Toe severely stubbed	3.5 × 3.5	Growing from under nail of left big toe	Papillomatous fibrotic tumor with branching and partly cystic eccrine sweat ducts; (eccrine equivalent of nævus syringadenomatosus papilliferus?)

openings. The entire area was excised deeply six months after the first operation; the wound was sutured and healed uneventfully. Three years later only two linear scars remained, and there was no recurrence. Histologic examination of the recrudescent lesion showed typical naevus syringadenomatosus papilliferus in connection with, by then, considerably hypertrophied deep-seated sweat glands.

During the following 10 years, biopsy material from pertinent cases was collected, most of it through the collaboration of a number of dermatologists and pathologists. Some of the patients were adults, some were children; some of the lesions were plain verrucous or sebaceous nevi, some were crusted papillomatous tumors. In addition, several other instances were seen at meetings or in consultation, without the opportunity of studying histologic material. Table 1 lists 31 cases with 32 lesions, all of which were examined microscopically, some of them by serial section. In the Table these cases are divided into three groups. The first 17 cases had fully developed papilliferous lesions (Fig. 3 *A*); the second group includes 14 verrucous epidermal nevi with more or less malformed pilosebaceous complexes, some of which deserved the designation of naevus sebaceus (Fig. 3 *B*). The third group is represented by only one case, that of a unique papillomatous tumor of the

TABLE 2.—*Age Distribution of Thirty-Two Organoid Nevi in Thirty-One Patients*

	Total	Postadolescent		Adolescent 15-12 Yr.	Pre-adolescent 11-6 Yr.
		Over 30 Yr.	29-16 Yr.		
Group 1					
With syringadenoma	17	9	8	..	..
Group 2					
Without syringadenoma	14	1	4	4	5
With apocrine glands	9	1	4	3	1
Without apocrine glands	5	..	..	1	4
Group 3					
Atypical eccrine tumor, toe	1	1	..	..	..

toe. In comparing the first two groups (Table 2), a striking age difference is found. None of the fully developed lesions arose before adolescence; 9 of the 17 patients were older than 30 years. In the second group, the ages ranged down to 6 years, and only 1 out of 14 patients was above 30. In the second group lesions may be subdivided in those which contained recognizable apocrine glands and those which did not. With the exception of one 10-year-old girl who possessed apocrine glands (Fig. 6 *B*), there is a division at the age of 12 years in this respect, and all patients older than 12 years had apocrine glands in their nevi. The significance of these facts will be discussed later on.

LIFE HISTORY

The history of these 30 patients (Table 3) shows that 15 had lesions at birth, and an additional 8 developed them in infancy or childhood. Twenty-one tumors were situated on the scalp; 4 on the face; 3 on the neck, and 1 each on the upper back, in the axilla, and on the abdomen. In only four cases was there a definite statement that no lesion had been present early in life. The first lesion was described as just a bald spot in 4 cases, as a smooth plaque in 7, and as papular or verrucous in 18. This last category might be smaller if carefully collected anamnestic data were available in all cases. Definite trauma preceded the development of the papilliferous lesion in 6 of the 17 cases, and a history of minor injuries by the comb, by rubbing of clothes, or by picking at the nevus was given by five patients.

The life history of Case 12 brings out most of the characteristic features of naevus syringadenomatosus papilliferus. This 23-year-old man had at birth a hairless, smooth area in the right parietal region of the scalp. The lesion extended from near the anterior hairline close to the vertex. During the first months of life, this area is said to have become eczematous and was treated for some time with sulfur ointments. Gradually an elevated plaque developed, and at puberty this became studded with yellow papules. When the patient was first seen, at the age of 16 years, there was a hairless area on the right side of the scalp measuring about 10 by 3 cm. There was an almost cerebriform elevated plaque consisting of gyrated coarse folds of dirty-yellow color and exuding a rancid odor. Numerous yellow spots, which obviously were large sebaceous glands, could be seen below the surface, which was mildly hyperkeratotic and greasy. The patient was advised that complete excision and plastic repair was the only way in which the nevus could be removed, but nothing was done until he returned, at the age of 23 years. The patient stated that after injury with the comb, a change had taken place in the nevus during the previous few months. There were two firm skin-colored nodules, each measuring about 6 mm. in diameter, superimposed on the gyriform elevations. These nodules

TABLE 3.—*Analysis of Thirty Cases of Groups 1 and 2*

Location of Tumor		Nature of Original Lesion		Age at Onset	
Scalp	21	Bald spot	4	Newborn	15
Face	4				
Neck	2	Smooth plaque	7	Childhood	8
Axilla	1				
Upper back	1	Papular or verrucous	18	Adult life	4
Abdomen	1	Unknown	1	Unknown	3
Total	30		30		30

were hyperkeratotic, with a horny plug in the center. One of them and the full thickness of the underlying skin was removed for biopsy. Serial sections (Fig. 4) showed large malformed pilosebaceous complexes beneath a papillomatous epidermis. Deep in the skin there were large sweat glands of apocrine type. The ducts of one of these as it approached the surface became hypertrophic and funnel-shaped and was lined with high columnar epithelium. A polypous structure protruded from the opening and formed the center of the keratotic plug which had been seen macroscopically. Here, again, there was development of a still microscopic papilliferous syringadenoma in an organoid, predominantly sebaceous nevus.

The life history of naevus syringadenomatosus papilliferus, as reconstructed from the study of these 30 cases, is as follows: The lesion is a hamartoma in the sense that there is a congenital circumscribed malformation of practically all the components of the skin. The epidermis; the pilary complexes, comprising hair, sebaceous gland, and apocrine gland; probably the eccrine sweat glands, and the connective tissue which subtends these epithelial structures, all are involved. The degree of involvement of the individual structures may vary, and with it the clinical manifestations. Scar-like bald areas, infiltrated plaques with or without prominent sebaceous glands, verrucous or papillomatous papules and nodules may be found as the primary lesion or may develop one from the other during childhood or puberty. Adolescence appears to be the turning point in many of these lesions. As in the normal skin, so in these nevi, sebaceous glands grow bigger and apocrine

glands reach maturity. There is no doubt that many lesions never progress beyond this stage. However, in a percentage of such organoid nevi, papilliferous proliferation occurs, which often follows trauma, such as incomplete superficial removal, accidental injury, or possibly, in the "spontaneous" cases, unnoticed minor traumatism.

This thesis is borne out by many of the published case histories, not all of which can be cited. It will, however, be appropriate to quote Stokes (1917),[7] who said of his case:

Since the lesion was apparently not congenital, it must be conceded that the adenomatous degeneration occurred in later life as an incident in the life history of the naevus. The mere

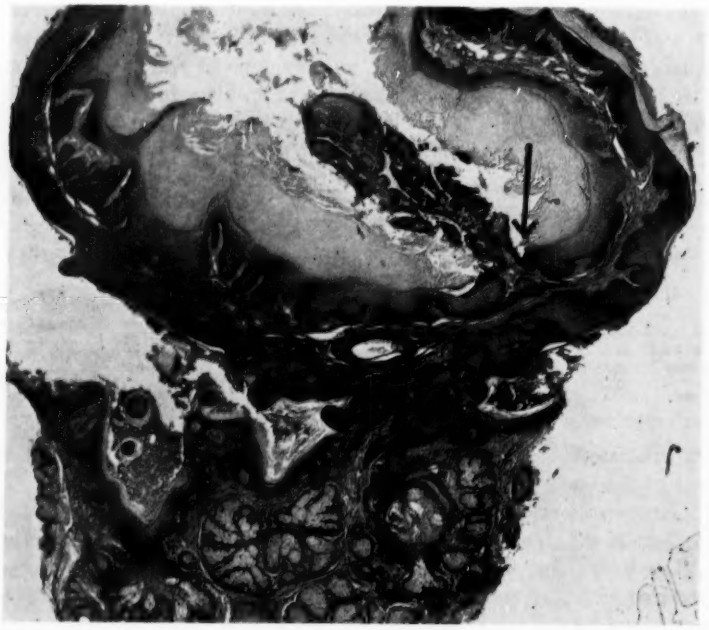

Fig. 4.—Largest portion of a section of the biopsy specimen in Case 12, showing papillomatous and sebaceous nevus. Apocrine glands present in the lesion are illustrated in Figure 5*A*. A cup-shaped papillomatous excrescence harbors a polypous structure in its center (base indicated by arrow), which represents a "hidden" papilliferous cystadenoma. × 14; orcein and Giemsa solution.

fact that adenoma developed in later life in a region presumably predisposed . . . to degenerative and neoplastic changes of this type need not, from the broader histogenetic standpoint, preclude the use of the term "Naevus syringadenomatosus."

HISTOGENESIS

Analysis of the 30 cases presented here bears out the principle of Stokes's dynamic concept of histogenesis, which was later stated in a similar manner by Woringer.[8] Yet certain modifications of the details of the thesis appear indicated. Stokes, writing before the distinction between eccrine and apocrine glands was established (Schiefferdecker, 1917[9]), spoke of sweat glands in general and favored

derivation of the adenoma from misplaced embryonic-cell inclusions. The latter hypothesis was elaborated recently by Lever,[10] who proposed derivation of all organoid epithelial skin tumors and of basal-cell epitheliomas from the primary epithelial germ which during ontogenesis produces hairs, sebaceous glands, and apocrine sweat glands. The present series suggests that most of these tumors are indeed related to the apocrine glands, but that in a few cases the eccrine glands are responsible wholly or in part. It is further suggested that the adenomas originate either from fully developed sweat glands or from pluripotential adult epithelial cells of the skin.

To take up the second point first, evidence for the pluripotentiality and interchangeability of the reproductive cells of adult epidermis and adnexa was collected in another paper.[11] It may suffice here to point to the restitution of epidermis from deep remnants of adnexal epithelium in any large denuded wound. Quite recently Montagna, Chase, and Melaragno[12] found that in the skin of hairless mice any isolated nest of follicular sheath cells will form sebaceous cysts which later become keratinized and epidermoid. Case 17 of the present series furnished almost experimental evidence for the derivation of the adenoma from adult structures. This was the case of the 16-year-old boy in whom papilliferous lesions developed after extensive cauterization of a papillomatous nevus. Sections in this case showed that the pilosebaceous complexes which were present in the first biopsy material had been completely destroyed and that the papilliferous cysts and sinuses connected the epidermis above with mature glands below. If they did not develop through proliferation of the latter, they must have been formed from epidermis which was "new," reconstituted epidermis covering the previously denuded surface. In order to maintain the hypothesis of embryonic-rest origin, one would have to assume that such rests were carried along through all the regenerative processes which led to epidermization of the defect, and that they then remained dormant for several months before the adenoma became apparent. As to the exact point of origin of the adenoma, whether it grows down from the epidermis, or up from the coil glands, or is formed by cystic dilatation of the ducts, observations in this series of cases suggest that all three possibilities are realized either singly or in combination in the individual lesions.

PARTICIPATION OF APOCRINE GLANDS

In regard to the type of gland from which these tumors are derived, it could be said that apocrine origin is unlikely because most of the lesions occur in regions, such as the scalp, where apocrine glands are not normally found (Anderson[1]). By applying the Turnbull blue reaction for iron according to Homma * to several of our tumors, I obtained direct proof of the presence of apocrine glands in five cases. In some cases the opening of relatively normal glands into the hair follicles could be demonstrated in serial sections (Fig. 5 *A*), and in at least one case early cystic change of such a duct was seen (Fig. 5 *B*). In other cases, however, particularly in those which showed cystic dilatation of the deep coils and absence of active secretory processes and in which no iron could be demonstrated, the decision remained in the balance. Often what appeared to be the duct of an apocrine gland was found opening on the skin surface. This, of course, is the rule once the tumor is fully developed and must be expected in all cases in which previous surgical

* References 13 and 14.

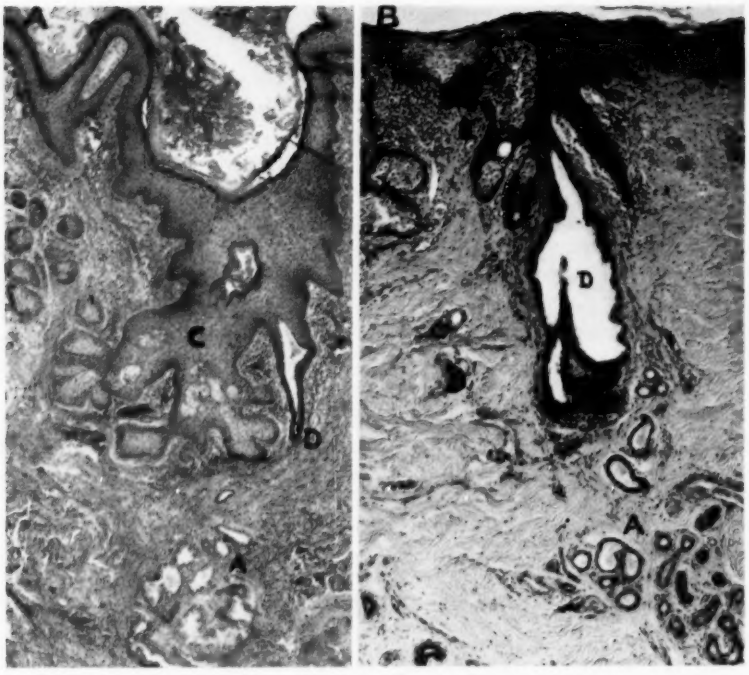

Fig. 5.—*A*, duct (*D*) of apocrine gland (*A*) opening into a malformed pilosebaceous complex (*C*) in Case 12. × 30; hematoxylin and eosin. *B*, cystic duct of apocrine gland opening into malformed pilosebaceous complex in Case 15. Eccrine duct (*E*) opening into epidermis. Plasma-cell infiltrate. × 45; hematoxylin and eosin.

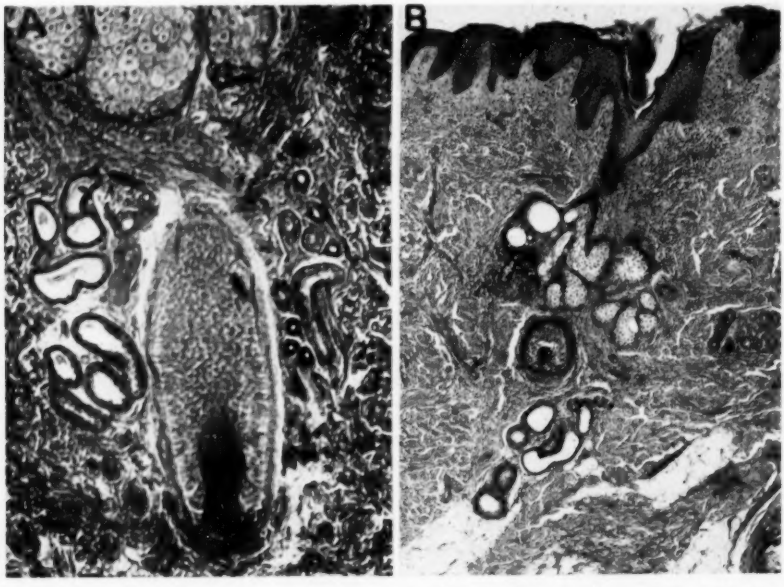

Fig. 6.—*A*, normal hair root and sebaceous gland in the first specimen of Case 17 (Lesion 17b). An eccrine gland can be seen to the right of the hair root. To the left, there is an apocrine gland, which is heterotopic for this region (nape of neck). × 90; orcein and Giemsa solution. *B*, malformed pilary complex with mature apocrine gland in a 10-year-old girl (case of Dr. I. Botvinick and Dr. L. W. Gardner, Case 25). An eccrine gland is shown in the right half of the picture. × 30; hematoxylin and eosin.

intervention has destroyed the superficially situated pilosebaceous structures. In such cases, less direct evidence has to be adduced. One argument in favor of apocrine-gland origin is the observation that practically all these lesions become active only after puberty, when these glands reach maturity. There are a few cases in the literature in which papilliferous tumors developed in young children (Sachs and Lewis,[4] Marcus and Wooldridge[15]), but these do not rule out an apocrine-gland origin. Apocrine glands may develop in nevi unusually early in life, as in Tappeiner's case of apocrine-gland nevus in a 4-year-old child in whom there were fully developed glands.[16] In principle, it is well conceivable that apocrine glands which are a normal part of the embryonic hair anlage all over the body may develop in regions where they usually regress if this region is the seat of hamartomatous disturbance. Kreibich's case,[17] perhaps the most extensive involvement of this type ever reported, with unilateral lesions extending from the posterior hairline down over the neck and shoulder to the right arm and breast, is an example of the widespread heterotopic development of apocrine glands in connection with the pilary complexes in an organoid nevus.[18] In the present series, apocrine glands were present in all postpubertal nevi which did not yet show papilliferous development (Fig. 6). Lastly, the restriction of histologically similar tumors to sites of apocrine-gland distribution, such as the vulva and breast, speaks for analogous derivation in our group. It may be noted that Case 2 of the present series had had a papilliferous cystadenoma (possibly a low-grade carcinoma) of the breast four years before the tumor on the scalp became manifest.

PARTICIPATION OF ECCRINE GLANDS

By coincidence, a papillomatous tumor with obvious sweat-gland participation was encountered (Case 31, Fig. 7 *A*) that had arisen near the nail of the big toe, that is, in a region free of pilary complexes. This tumor exhibited interesting similarities and differences (Fig. 7 *B*). There was dense fibrous stroma covered with hypertrophic epidermis. There were branching sweat ducts extending from the epidermis, and there were accumulations of plasma cells, which are so typical of naevus syringadenomatosus papilliferus. However, instead of papilliferous sinuses lined with high columnar epithelium, the branching ducts here consisted of multiple rows of epidermoid cells, and the lumina were unusually narrow, widening out only occasionally. A definite cuticle often lined the lumen. While this lesion could not be diagnosed as naevus syringadenomatosus papilliferus, it seemed to constitute an analogous development of eccrine ducts and led to a search for similar features in our series.

Again, it was Case 17 which furnished the looked-for evidence. One of the newly formed papules of the recrudescent nevus shows in its substance eccrine, as well as apocrine, ducts ascending toward the epidermis from their respective coils. The apocrine ducts widen out into papilliferous sinuses lined by high columnar epithelium (Fig. 8 *A*), while the eccrine ducts, lined by cuboidal cells and showing a cuticle, usually open with a narrow, normal pore. One of the eccrine ducts, however (Fig. 8 *B*), merges into a maze of branching solid or hollow strands of rete-like cells which duplicate the picture found in the tumor from the toe. This appears to be definite proof that eccrine ducts can participate in the formation of naevus syringadenomatosus papilliferus, but, owing to their different construction, form different structures. This view is confirmed by Case 6, which has the typical history and

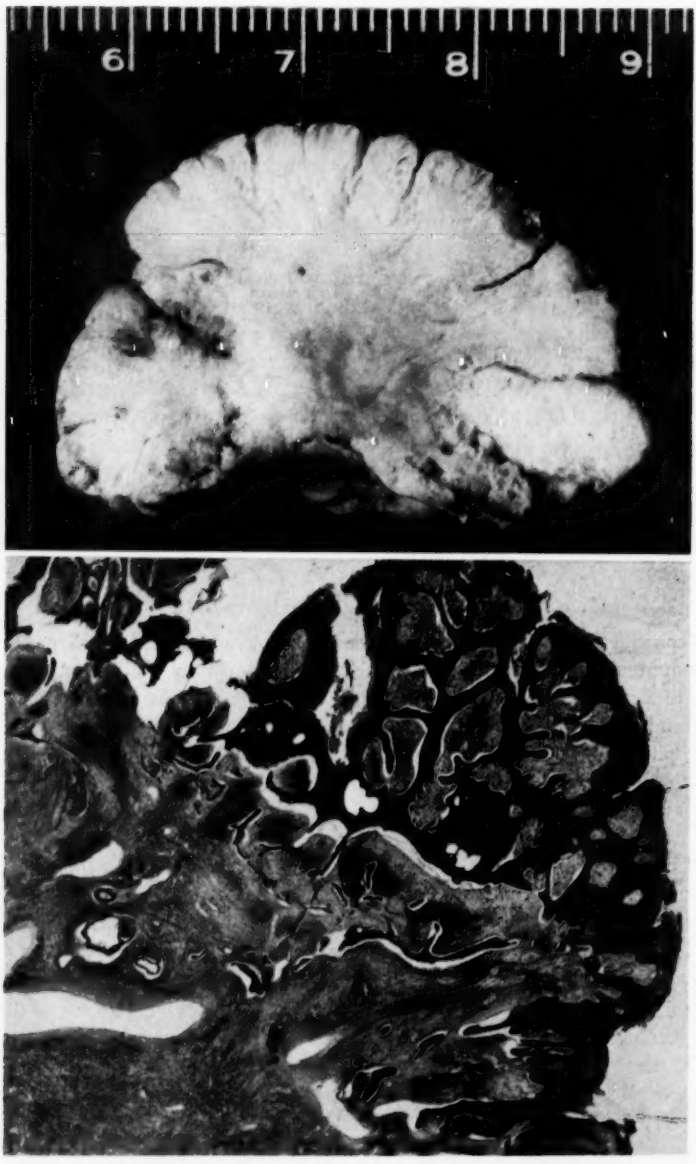

Fig. 7.—Papillomatous tumor, with participation of eccrine ducts from the toe of a 55-year-old man (Dr. William L. Poole's case, Case 31). *A*, cut surface of the gross specimen, enlarged two and one-half times, as shown by the metric scale. *B*, section stained with hematoxylin and eosin; × 8. Some of the branching and dilated ducts are shown in the fibrous core of the tumor. The empty spaces also contained cystic ducts, which were lost in the preparation of this section.

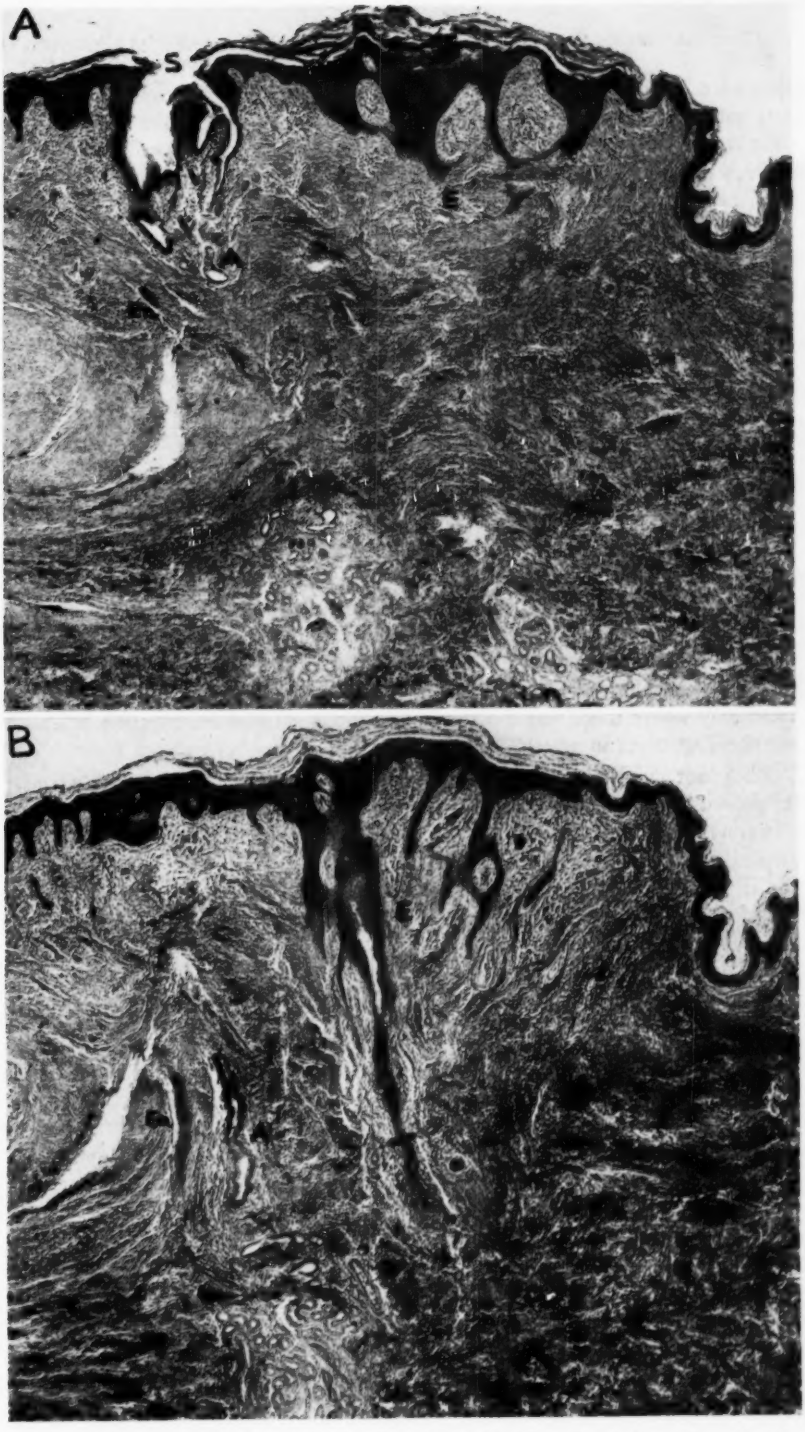

Fig. 8.—Two sections of a series illustrating the participation of apocrine and eccrine ducts in the recrudescent lesion of Case 17 (Lesion 17a). *S* indicates a papilliferous sinus, into which an apocrine duct (*A*) opens; *E* indicates the maze of stratified epithelium into which an eccrine duct opens; *En* indicates a normal eccrine duct. Note the atypical fibrous stroma of the papule. × 28; *A*, hematoxylin and eosin; *B*, orcein and Giemsa solution.

appearance of naevus syringadenomatosus papilliferus, but in which branching ducts with thick cuticle and cuboidal cells form the substance of the tumor. Eccrine origin is suggested in some published cases (Eljasz,[19] Dörffel,[20] Case 3 of Wolters [21]) in which the authors report that the sinuses were lined with epidermoid cells. Such origin can be considered certain in Anderson's case from the sole.[1]

The histogenesis of the adenomatous part of naevus syringadenomatosus papilliferus, as deducted from the present series, may then be summed up as follows: On the basis of hamartomatous malformation of the skin, and after puberty has set the stage through maturation of apocrine glands, these mature glands or pluripotential cells in the adult epidermis are stimulated to adenomatous proliferation by trauma or unknown causes. Occasionally, eccrine glands participate or form analogous tumors with somewhat different characteristics.

ACCESSORY FEATURES AND COMPLICATIONS

The clinical and histologic picture of naevus syringadenomatosus papilliferus presents several other peculiar features which deserve short discussion.

The combination of naevus sebaceus with papilliferous syringadenoma has occasionally been claimed to be exceptional (Grund [22]). This series of cases suggests that the presence of more or less malformed pilosebaceous complexes is obligatory, as it furnishes the hamartomatous foundation in which the adenoma develops. Whether the sebaceous glands are so hypertrophic that they deserve the designation of naevus sebaceus is of secondary importance. Pilosebaceous complexes were absent only where there was a history of previous surgical intervention or in some long-standing cases in which secondary involution may have taken place.

Malignant degeneration of the adenoma was not encountered in this series. It was proved beyond doubt only once in the literature (Hedinger [23]). Nödl [5] reported infiltrating malignant growth in one of his cases. On the other hand, Case 15 showed independent development of basal-cell epithelioma in the nevus at an early age. Similar instances were reported by Reuterwall [3] and Hval.[24] Pilary complexes of such degree of malformation that they suggested early trichoepithelioma were encountered in several of our cases.

Werther's case, from which the designation naevus syringadenomatosus papilliferus is derived, contained nests of nevus cells. Few other cases (Sachs and Lewis [4]) presented this feature. In the present series, nevus cells were found only in Case 27, which was an organoid nevus of papillomatous structure in an 11-year-old boy.

A prominent feature in most of the lesions was the presence of large numbers of plasma cells. This feature has been mentioned consistently in the literature. In at least two cases (Hedinger,[23] Stokes [7]) it assumed such proportions that it was considered to be an independent development (granuloma by Stokes, plasmoma by Hedinger). In this series plasma cells were present in variable numbers, but were practically never absent. They were even present in some cases which did not yet show the papilliferous adenoma (Case 19). The constant occurrence of plasma cells in a nonmalignant and noninfectious lesion is curious in view of the role which recently has been attributed to the plasma cell in antibody formation. It has been claimed that those diseases are characterized by plasma-cell infiltrate that show high serum-globulin levels. It is hard to conceive of any immunologic

role of the plasma cells in these nevi. Mast cells, which also have been reported by some authors, were often present in the lesions in our cases, but never in excessive numbers, and usually not more than one might find in any kind of nevus.

Finally, something should be said about the stroma. Not only the epithelial structures, but also the connective tissue, showed considerable changes in these tumors. The normal architecture of the corium was replaced by abnormal fibrous tissue, even in an almost microscopic lesion such as that in Case 3. This feature indicated that the papilloma was not just a skin tag, but was part of the general hamartomatous disturbance. The papillomatous configuration of many of the other tumors supports this view. The connective tissue which formed the stroma of the recrudescent nodules of Case 17 was not ordinary scar tissue, but was more highly organized, with fine new elastic fibers between the collagen bundles. It may well be asked whether the altered connective tissue may not have an inducing influence on the predisposed epithelial structures in these nevi. Abnormal hair papillae which induced abortive hairs in excessive numbers were found in several cases. Other aspects of the question of epithelium-connective tissue relations in skin tumors have been discussed in a previous paper.[11]

TREATMENT AND DIAGNOSIS

It is obvious from the foregoing discussion that complete cure of naevus syringadenomatosus papilliferus can be expected only if the entire involved area is excised through the full thickness of the skin, including that part of the subcutaneous fat which contains the deep-seated apocrine coils. Even if that was done, recurrence or, rather, development of new lesions in the same area was reported by some authors (Dörffel,[26] Balog [27]). Even in cases of seemingly simple papillomatous nevi, complications may be encountered if the area harbors heterotopic, but otherwise normal, apocrine glands, as in Case 17 of this series (Fig. 6*A*). Clinically, satisfactory results were reported by the attending dermatologists in several cases of this series after ablation of the papilliferous portion and desiccation of the base. The time of observation in these cases usually was short, and if lessons can be learned from the literature, later recrudescence of the cystadenoma is far from unlikely. Recurrence, and even exacerbation, after surgical intervention was seen in 5 of the 17 cases. It may be mentioned that radium and x-ray treatment was advocated by some authors (Hval,[24] Reuterwall [3]).

It is noteworthy that the diagnosis of naevus syringadenomatosus papilliferus was not suspected clinically in 16 out of 17 cases. The exception was Case 12, which was observed at a time when my alertness had been stimulated by previous experience. The question of malignant change in a nevus was raised repeatedly by the clinician, but only once correctly. In Case 15, a basal-cell epithelioma was associated with the hamartoma. As previously mentioned, the incidence of malignancy is apparently very small in this type of nevus. It is hoped that the presentation of this series of cases will call the attention of dermatologists to a fairly typical train of events and will be of help in future diagnosis.

SUMMARY

Thirty-one cases are presented in an attempt to analyze the life history of naevus syringadenomatosus papilliferus. Seventeen tumors were fully developed papilliferous lesions, although some were of subclinical size, while 14 were organoid nevi

in children and young adults. It is concluded that in naevus syringadenomatosus papilliferus the adenomatous development is always secondary to a hamartomatous disturbance of the entire cutaneous area, but that the papilliferous structures are derived from mature apocrine glands (in occasional cases from eccrine glands), not from embryonic rests. The role of puberty and trauma in the provocation of the papilliferous change is discussed.

ABSTRACT OF DISCUSSION

Dr. Marcus R. Caro, Chicago: Photographs of lesions of naevus syringadenomatosus papilliferus are so rare that I am taking the liberty of presenting a slide of the only one we have in our collection.

The patient was a white woman, aged 42, who was seen in 1948, with a quarter-sized verrucous patch on the back of the scalp. This had first appeared at the age of 12 after a blow by a metallic object, and it had but recently developed a pea-sized soft granulomatous central papule that bled readily after combing or other slight injury. A clinical diagnosis was made of verrucous nevus with a superimposed granuloma pyogenicum.

The granuloma was removed for examination, and the rest of the patch was destroyed by electrocautery. The histopathologic examination, of course, gave us the correct diagnosis of naevus syringadenomatosus papilliferus. The patch remained crusted, and when the patient was seen a year later, it again had a small central soft granulomatous papule. That is how we had the good fortune to obtain a photograph of the lesion before excising it deeply, and this time apparently successfully. Sections from both the original lesion and the recurrent one were diagnostic of naevus syringadenomatosus papilliferus, with a vascular stroma containing a dense cellular infiltrate, including many plasma cells.

Dr. Pinkus has given us a welcome contribution in his painstaking histopathologic study of 31 cases of naevus syringadenomatosus papilliferus. This series, and the cases diagnosed in our laboratory, are proof that this tumor is not as rare as a perusal of the literature would seem to indicate. It is a truism that one sees only that which he recognizes. Of naevus syringadenomatosus papilliferus it may well be said that many are eyed but only few have been seen. I feel certain that Dr. Pinkus, by demonstrating so many histopathologically proved cases, has helped us to be able to correct that discrepancy in the future.

While these tumors may originate from apocrine glands, I agree that we cannot exclude the eccrine glands from an occasional parental relationship. In addition, the hyperplasia of the lining cells to produce papillary ingrowths of both epithelium and stroma is no doubt partly the result of trauma, for these lesions occur principally on accessible parts and they are often activated by some injury. That the stroma takes an active part in the production of these lesions has been indicated to me in a number of cases I have studied, in which the proliferation of the blood vessels was so great as to suggest at first the histopathologic diagnosis of granuloma pyogenicum.

We should all have a high index of suspicion of the diagnosis of naevus syringadenomatosus papilliferus when confronted by a tumor that is verrucous, crusted, or vascularized, that is seen on the scalp, face, or neck, that has been present in some form since childhood, and that has undergone some change at puberty or particularly after injury. It is perfectly true that these specifications apply equally well to many other tumors. It is equally obvious that no definitive diagnosis of skin tumors can be made without a biopsy.

Statistical studies in diseases of the skin can have value only when they are based on uniform data. To give any validity to statistics of tumors of the skin, such as the relative incidence of certain tumors, one must have histopathologic confirmation in every case. In studying infrequently recognized lesions, such as naevus syringadenomatosus papilliferus it would be helpful if all cases of tumors of the skin were described minutely, photographed in color, and then examined histopathologically. Only in this way can we make it possible to restudy the clinical features of each case on the basis of histopathologic sections from cases that had not been recognized before removal. Such a reappraisal of each proved case of naevus syringadenomatosus papilliferus would have great value in teaching us better to recognize these lesions in the future.

DR. LOUIS H. WINER, Beverly Hills, Calif.: I was very happy to see this paper listed in the printed program of this meeting because it made me aware of this type of tumor occurring after trauma to an epidermal nevus.

Recently, I studied the slide of a syringocystadenoma in a 7-year-old patient who four years previously had a skin tag cauterized. At the site of cauterization a tumor recurred and had increased in size. Some of the general pathologists are unaware of this entity, since it was diagnosed carcinoma histologically.

DR. HERMANN PINKUS, Monroe, Mich.: I thank Dr. Caro and Dr. Winer very much for their discussion. Both cases mentioned in the discussion emphasized the point that I hoped to make in my presentation, that is, that these changes usually occur secondarily in a nevus, in a lesion that has been present for a long time.

Dr. Winer's patient was a 7-year-old girl: that is, the syringadenoma here developed before puberty, and there are a few such cases reported. For instance, two of the five cases of Sachs and Lewis were of young children. While this occurrence may seem to argue against apocrine-gland origin, one must remember that apocrine glands may develop prematurely in nevi, as in Tappeiner's case, which is mentioned in the text.

I have nothing to add except once more to express the hope that this presentation may help to recognize this tumor oftener and to treat it in a rational manner.

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PITYROSPORUM OVALE TYPES CULTURED FROM NORMAL AND SEBORRHEIC SUBJECTS

HERBERT J. SPOOR, Ph.D., M.D.
EUGENE F. TRAUB, M.D.
AND
MARY BELL, B.S.
NEW YORK

CONVINCING proof of an other than casual association of the Pityrosporum ovale (bottle bacillus) group of organisms with seborrheic conditions has not been fully established. Some recent investigators have emphatically asserted an etiological relationship, while others have denied its existence. The majority of workers concede only a possible pathogenicity to the organisms, even though a close association with seborrheic infection has been repeatedly observed. Technical difficulties in culturing the organisms and maintaining them through sufficient subcultures to obtain pure strains account for much of the lack of certainty about their status. The organisms show extreme pleomorphism when studied by direct mount, and this plus the invariable presence of contaminants in the seborrheic scale has caused confusion.

Since the report of Moore and colleagues, in 1936, which proved that some strains of the organism could be consistently grown on selected media, many cultural improvements have been made. Benham's use of oil fortification of the medium after her recognition of the lipophilic nature of the fungus and the discovery of several growth stimulants for the group has led to development of a culture medium which not only induces a high percentage of positive primary cultures but also prevents or inhibits the growth of interfering contaminating organisms. Subcultures are now more readily maintained, although isolation of pure cultures of the individual types within the Malassezia group remains technically difficult.

Utilizing these improvements in media and employing some novel scalp- and skin-sampling techniques, we have cultured material from the scalps of several hundred adults and children. We have isolated one or more types of P. ovale organisms from a very high percentage of the cases. The frequency of positive culture and the character and body distribution of the types isolated from these normal and seborrheic subjects may help clarify the clinical role of the group.

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From the Department of Dermatology, New York Medical College; Dr. Eugene Traub, Director (Dr. Spoor); and the New York Medical College-Metropolitan Hospital Research Unit; Dr. Thomas H. McGavack, Director (Miss Bell).

METHODS

Medium.—Culture material consisted of a wort-agar medium fortified with oleic acid (1.5%) and the growth stimulants sodium ethyl oxalacetate (0.5%) and thiamine (0.1%). This medium was selective for and stimulating to the P. ovale types. It inhibited bacteria and permitted only the occasional growth of some mold contaminants. Lipophilic yeasts similar to the Malassezia could grow. Subcultures were frequently grown for periods in an atmosphere of 10% carbon dioxide in order to give them vigor. After isolation, some strains could be maintained for periods on Sabouraud's medium, but without occasional passage through the oil-wort medium these isolates lost vigor.

Sampling.—Scalp sampling was done with a stiff sterile toothbrush, which scraped vigorously through the entire scalp. Sufficient pressure was applied to release adherent scale. The brushing gathered a consistent representative sample of whatever organisms were present on the scalp. After sampling, the loaded brush was dropped into a sterile test tube containing sufficient sterile distilled water (60%) to bathe the bristle adequately. The tube was stoppered and agitated vigorously. Aliquots of solution were plated for cultivation and study. For convenience in sampling, male subjects were used almost exclusively. Samples taken from areas other than the scalp were obtained by the same brushing technique, but where hair was not present the pressure applied to release adherent debris was much less.

BACTERIOLOGICAL FINDINGS

Conservatively, the P. ovale group can best be classified as that group of degenerate fungus-like bacterial organisms which at some stage exhibit a characteristic "bottle" or "flask" shape, and which require a highly fortified, oil-enriched medium for primary culture. We have consistently isolated four strains of these organisms. Three of these strains are apparently identical with previously reported types, and the fourth is probably a new isolate. For convenience, our organisms have been designated as Types 1, 2, 3, and 4 (Fig. 1). Types 1 and 2 are culturally and morphologically identical with the American Type Culture Collection isolates 7253 and 7132, which we obtained for comparison from their stocks. Type 3 is the new isolate obtained during this study, and Type 4 is apparently identical with the organism reported by Moore and referred to fully in the description by Lewis and Hopper. With Petri dish culture the several types are readily differentiated. The most striking difference is the color of the colony, varying by type through tan, white, black, and salmon-pink. The types may be described as follows:

Type 1. Light tan color, turning slightly darker within a few days. Colony is smooth, glistening, and moist. Individual colonies, small in size, not exceeding 4 mm. in diameter.

Type 2. Bright white, turning gray as colony ages. Colony is dry, dull, and wrinkled. Small in size.

Type 3. Often resembles Type 1; light tan for a few days, then turns black. Color change persists until entire colony is jet-black. It is smooth, glistening, and moist, much later becoming dull and dry.

Type 4. Initially colony is smooth, glistening, and moist, resembling Type 1; then it develops radiating ridges to the periphery, rough surface with a few small outgrowths. The color is dull and varies from a light salmon hue to a pinkish buff.

Morphologically, there was a decided similarity in the cells of the several types. There seemed to be a slightly closer relationship between Types 1 and 4 and Types 2 and 3. Although pleomorphism in the group was the rule, certain resemblances only became apparent when the organisms were grown on liquid and solid media

and observed in the wet- and dry-mount preparation. These comparisons of pleomorphic forms are shown in Figure 2. Marked morphological differences are seen, not only between the types but within the groups of each type. The individual specimen shows sufficient variation to prove that pleomorphism is inherent in the organism and not solely induced by choice of medium. In general descriptive terms, the cells vary in size from 3 to 15 μ; most of them are from 4 to 5 μ in diameter. There are many budding cells, resembling bottles or gourds. The larger cells are

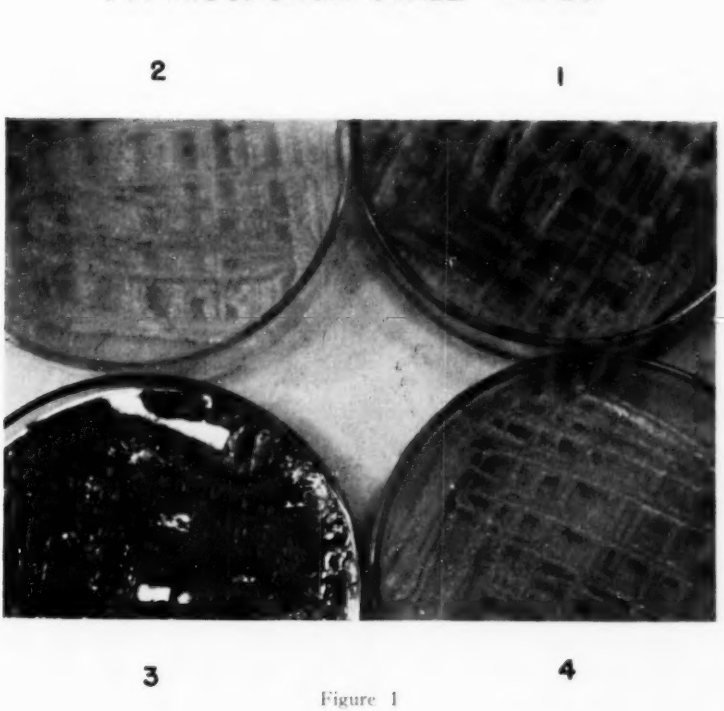

Figure 1

apparently encapsulated with some gelatinous material. Small chains and occasional double-headed cells are seen. Actively budding cells generally are of the smaller types, and the resting cell tends to assume a spherical or hexagonal form.

The several group types shown are not the only ones obtained by primary isolation. We have frequently isolated seemingly new species which subsequently have developed similarity to one of our accepted groups. In the clinical studies which follow, these unidentified strains are classified as "yeast-like types" and statistically have been considered not to be P. ovale. Such conservative treatment of the data may not be necessary, particularly as the entire group is so fluid. Efforts to attribute clinical significance to colonial or morphological variants of the general type, although frequently made, do not seem to be justified.

CLINICAL CONSIDERATIONS

We have cultured the scalps of many persons—men, women, and children, and have obtained one or more types of P. ovale organisms in a high percentage of the cases. This report gives data obtained primarily from men and boys, because short hair made for easier sampling. The positive cultures obtained were classified according to type. This separation was on colonial grounds and was made after 72 hours of incubation (36 C.) on the wort-agar medium. Only the P. ovale types grew on this medium. Control plates of nutrient agar and Sabouraud's agar showed the invariable occurrence of a white Staphylococcus and the occasional presence of

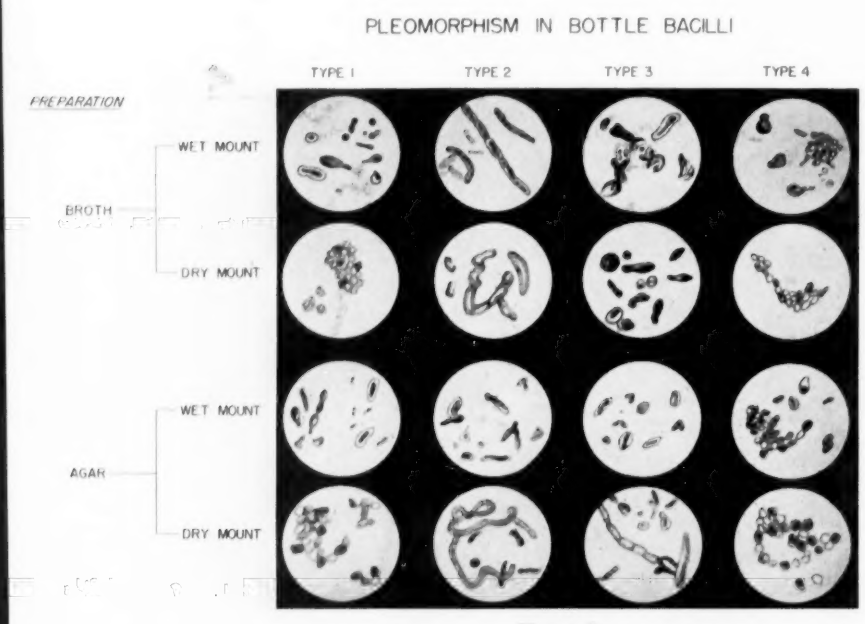

Figure 2

other bacteria and contaminating air-borne molds. Fungi were found only on the scalps of children with known cases of tinea capitis. These organisms did not grow on the special wort-agar medium. The frequency of occurrence and the type distribution of positive P. ovale cultures obtained from the scalps of 196 normal male persons chosen from office personnel working in the city is shown in Figure 3. The positive-culture frequency figure of over 60% compares very favorably with that reported earlier from direct-smear estimations. This speaks well for the vigorous sampling technique, as the figure is much higher than the one previously obtained. We did not compare direct-smear with the brush technique in this series. In 54.6% of the cases the organism isolated was identified as one of the four types previously discussed. Mixed cultures were frequently encountered, and 33% of the positive persons harbored the unidentified white yeast organism. Our Type 1 (A.T.C.C. 7253) was the most frequently identified, followed by Types 4, 2, and 3. The

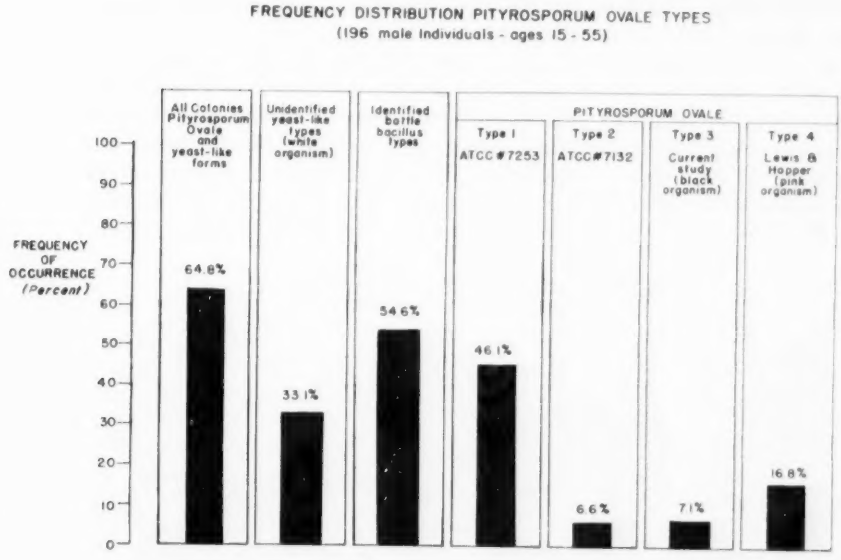

Figure 3

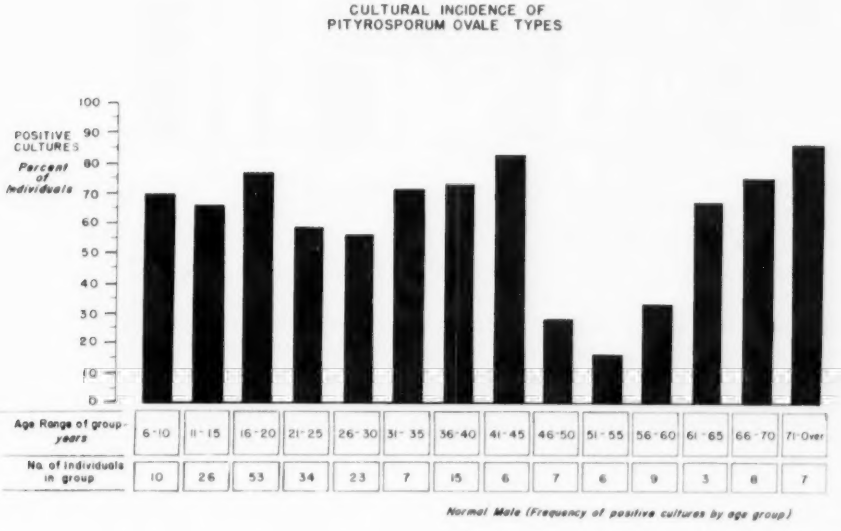

Figure 4

unidentified group may contain organisms of the A.T.C.C. 10969 * or 10972, the Pityrosporum orbiculare reported by Gordon. We have not checked this, because only the two types, A.T.C.C. 7253 and 7132, were available.

It has been stated that there may be a direct relationship between the level of circulating male hormone and the possibility of scalp infection with P. ovale, the impression being supported by the reported infrequency of infection of the prepubertal scalp. We have studied the cultural incidence of P. ovale types in 214 males ranging in age from 6 to 80 years. The data are shown in Figure 4. The positive-culture incidence was consistently over 50 to 60%, except for the age group of 46 to 60. Possibly the impressive drop in frequency of infection can be explained

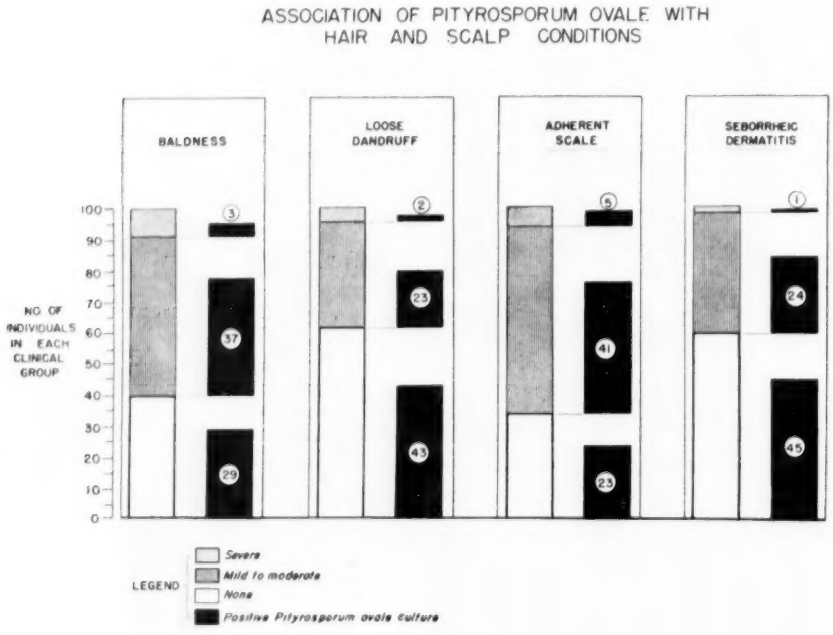

Figure 5

by greater attention by the subject to scalp care during this particular period. Expansion of the number of persons in each group might disclose a hormone-influenced trend at both 46 to 60 and 20 to 30 years of age, but there are too few cases here to warrant speculation. It can be definitely stated that there is no decrease in incidence of infection at either the pediatric or the geriatric extremities. Some of the children were obtained from a child-care institution and some of the older men from a geriatric hospital. The majority of the subjects were not from institutions.

Association of Positive Pityrosporum Culture with Hair and Scalp Condition.—During this study 100 young men had a rather complete record kept of the condition of their hair and scalp at the time of sampling. The components judged were the

* American Type Culture Collection: Personal communication to the authors.

extent of baldness, amount of loose dandruff, quantity of adherent scale, and the presence or absence of seborrheic dermatitis. The conditions were graded as none, mild to moderate, and severe. Attempts were made at quantitation of the examination estimates. For example, baldness was graded as follows: 0 to 5%, none; 5 to 25%, mild to moderate, and over 25%, severe. Figure 5 shows the observed data. The black columns show the number of persons in each grade and category with positive cultures for Pityrosporum. Many of the subjects with no evidence of hair loss, dandruff, or seborrhea showed positive cultures for the organisms. The most apparent correlation in these data is that an increase in adherent scale is associated with an increased frequency of positive culture.

TABLE 1.—*Seborrheic Dermatitis Cases—Body Distribution of Pityrosporum Ovale*

Case Identity			Areas of Seborrheic Involvement	Pityrosporum Ovale Types, Positive Cultures			
Initial	Sex	Age		Scalp	Ear Canal	Chest	Axilla
F. S.	M	46	Generalized dermatitis	..	..	4	1
J. B.	F	21	Scalp	..	1	..	..
J. M.	M	23	Moderate, scalp and chest	1	..	1	..
D. A.	M	30	Moderate, scalp and chest	4 and ?	..	4	..
F. C.	M	52	Severe generalized dermatitis	1	..	1	1
S. B.	M	35	Scalp and chest	3	..	..	..
H. S.	M	40	Scalp	1	..	..	..
R. S.	M	36	Scalp, chest, axilla	4 and ?	..	2	..
W. M.	M	57	Generalized dermatitis	..	..	..	..
E. A.	F	36	Scalp	1, 2, 3	3	..	..
D. S.	M	29	Scalp	3 and 4	..	..	..

TABLE 2.—*Pityrosporum Ovale (Type) in Domestic Animals*

Animals Used	
Dog 1 (household pet)	1, 4, and unident. yeast
Dog 2 (laboratory)	1
Cat 1 (household pet)	1, 2, 3, 4
Cat 2 (laboratory)	None
Cat 3 (laboratory)	1
Cat 4 (laboratory)	1
Horse 1 (saddle)	1, 3, and unident. yeast
Rabbit 1 (laboratory)	None
Rabbit 2 (laboratory)	None

Association with Seborrheic Dermatitis.—A small group of patients clinically diagnosed as having seborrheic dermatitis were studied to determine the frequency of occurrence of positive P. ovale cultures on areas of the body other than the scalp. The other suspect areas examined were the external ear canals, the axillae, and the chest. The organisms were very consistently present on the scalps, either in single or in multiple types. The next most frequent site of infection was the chest. The ear canals showed positive culture in 2 of the 11 patients (both women with mild seborrhea) and the axillae in 2 (both men with severe seborrhea). There was a reasonable uniformity of infection type in the several areas. The sampling technique was painful in the nonscalp areas, but all persons showed positive culture for the common gray Staphylococcus; therefore one can assume sampling proficiency. The foregoing data are shown in Table 1.

Induction of Seborrheic Lesions.—We did not attempt to produce seborrhea-like lesions in man by the use of our organisms. This step has been repeatedly attempted

by others. We did try to produce lesions by intradermal injection of active cultures into cats. Here we had fair success, particularly with the Type 4 organisms. We were unable to produce the lesions in rabbits. Because the results of these studies were inconsistent with other reports, we decided to look for the organisms on various domestic animals. We found Pityrosporum types apparently indentical with those found on man on the dog, cat, and horse. The organisms were not found on the rabbit. These studies are given in Table 2 and, although not very extensive, do show that the organism is not limited to man, even though a characteristic seborrheic dermatitis may be.

SUMMARY AND CONCLUSIONS

Use of special media, fortified to enhance their growth, has enabled us to obtain a high culture incidence of P. ovale types from human subjects.

The P. ovale types are several and may be separated by cultural means.

Identification is best made by colonial characteristics because organism pleomorphism transcends the types.

An over-all incidence of greater than 60% positive cultures attests to the frequency of Pityrosporum infection in man.

Suggestive age susceptibility may be indicated by these data.

Because as many persons without signs of seborrheic infection as with signs harbor P. ovale organisms, a causal relationship may be doubted.

The Pityrosporum organism is not confined to the scalp, nor is it limited to man in its distribution.

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DISTRIBUTION OF SKIN DOSES OVER SCALP IN THERAPY OF TINEA CAPITIS WITH SUPERFICIAL X-RAYS

JOHN S. STRAUSS, M.D.
AND
ALBERT M. KLIGMAN, M.D., Ph.D.
PHILADELPHIA

THE DEPILATORY effect of superficial x-rays is curative in almost all cases of epidemic tinea capitis due to Microsporum audouini. In this country the Adamson-Kienböck method of administering the radiation has achieved widespread usage. The radiation is delivered over five unshielded focal points which are approximately 5 in. (13 cm.) apart. Earlier investigators have noted that it is not possible to achieve a uniform dosage when irradiating a spheroid object such as the scalp. In the Adamson-Kienböck technique, a considerable degree of overlapping occurs in the regions between the focal points. For this reason there is a significant disparity in dose between the radiation received at the focal points and in the areas of greatest overlap. The use of this method would involve a decided risk if the quantity of radiation absorbed in the areas of overlapping could be shown to approximate the dose required for permanent hair damage (the permanent alopecia dose). Although this latter dose is not known for superficial x-rays, certain radiologists are sufficiently fearful of the potential damage of the Adamson-Kienböck technique that they have devised a new method in which overlapping is prevented by shielding each of five areas.

Nonetheless, experienced therapists who have treated thousands of cases consider the Adamson-Kienböck method to be safe and expedient. Still, those who use this method routinely must support their trust with knowledge. For this reason we have attempted to supply accurate data on the doses actually received by the scalp skin in different areas.

The previous works which have dealt with this issue have a limited value either because of insufficient technical details or because of intrinsic methodological deficiencies. Schreus and Proppe mathematically estimated that certain areas would probably receive twice the dose of the focal points (Adamson-Kienböck method, target-skin distance [TSD]—24 cm.). They did not indicate whether or not their sketch showing the main areas of overlap was based on actual experimental study. Details of their calculations are omitted and our results do not bear out their findings in the overlap areas. Epstein's epilating method consists of delivering the radiation to five points placed around the circumference of the scalp. He calculated that with a TSD of 30 cm., certain intermediate regions would receive one and one-half to

From the Department of Dermatology (Donald M. Pillsbury, Professor), University of Pennsylvania School of Medicine.

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two times as much radiation as the focal points. To our knowledge, Osborn, Tavener, and Farmer have been the only previous investigators to undertake a quantitatively defined experimental study of this problem. Although they have given precise methodological details for measuring the radiation and have plotted the actual skin doses rather than air doses, unfortunately they have not described their epilating procedure other than to remark that they use the five-field technique of the Middlesex Hospital. They inserted small ionization chambers into 48 holes distributed over half of a wax model of a child's head and then plotted the isodose contours. The regions of highest skin doses occurred in a triple overlap area occupying about 1 sq. in. (2.5 × 2.5 cm.) and located on either side of the vertex about 2 in. (5 cm.) from the midline. These areas received 1.6 to 1.7 times as much radiation as the focal points. They also have described in the occipital region a high dose area representing a double overlap. Their results are so divergent from our own that it seems possible that they did not use the Adamson-Kienböck technique.

MATERIALS AND METHODS

The measurements were made with a modified phantom of a scalp. A human skull was completely filled with a paste of the following composition: starch, 40%; flour, 40%; glycerin, 20%; water, sufficient quantity to yield a plastic material. The same paste was molded over the outside of the skull in a layer approximately 1 cm. thick. This depth was found by actual measurement to correspond to the thickness of the soft tissues overlying the calvarium of children. The greatest circumference of the molded phantom was 20 cm. This value likewise approximates actual measurements on children. This paste has approximately the same absorption and scattering characters as soft tissue.

The frontal focal point was established 3½ in. (8.8 cm.) above the glabella in the midsagittal line. This would correspond to the actual frontal focal point of the Adamson-Kienböck technique. The other four focal points were then marked out 5 in. (12.7 cm.) from each other according to the method outlined by MacKee and Cipollaro. In order to record the doses received at various points over the phantom, a grid was marked out in the following way: A point along the midsagittal line 2 in. (5 cm.) above the glabella was established. Posterior to this, points 1½ in. (3.8 cm.) apart were marked out along the midsagittal line. The skull was placed so that the inferior orbital plate lay in a horizontal plane; then parallel perpendicular lines were dropped from the points established along the midsagittal line. Along each of these perpendicular lines starting at the midline, points 1½ in. apart were marked out. The final pattern was a right angle grid with all the points along any line 1½ in. apart. The designation of these points is shown in Figure 1. The amount or radiation received at each point when the radiation was delivered to a particular focal point was measured by inserting a thimble chamber into the paste so that the midpoint of the chamber was level with the surface; in other words, half of the chamber was in the phantom. For each of the five focal points, the chamber was moved successively to every point on the grid. With the chamber in place at a given point, 100 r in air was administered to the focal point. The total radiation at each point was simply the sum of the determinations made with each of the five focal points. A Model 70 Victoreen condenser r-meter with a nylon thimble chamber was used. During the measurements the chamber was detached from the charging unit. As indicated above, the dose given was measured in air; under the experimental conditions with the ionization chamber on the phantom the doses were recorded directly as skin doses. The skin, or surface, dose recorded in this fashion approximates the aggregate tissue roentgen dose. It represents the sum of the radiation absorbed from the primary beam and scattered radiation for all five fields. Scatter is the difference between the dose in air and the dose with the ionization chamber on the phantom, the distance between the target and the chamber being the same in each case.

It is realized that for measurements of this kind, thimble chambers have inherent errors. These can be minimized by the use of extrapolation chambers. Quimby and colleagues have pointed out that in a region of maximum back-scatter with beams having a half-value of 0.5 mm. of copper, the thimble chamber and the extrapolation chamber give results which are in

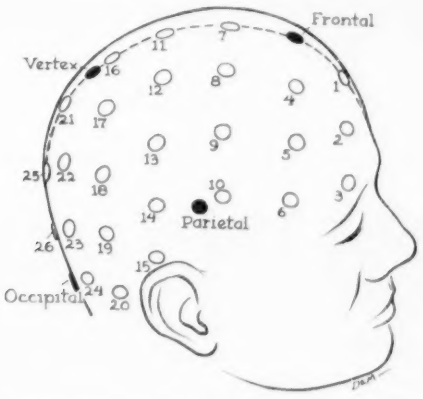
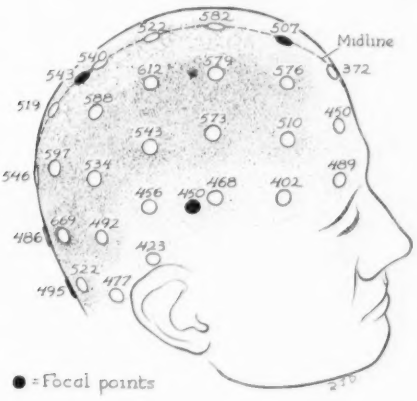


Fig. 1.—Diagram to show the position of points on the grid used.



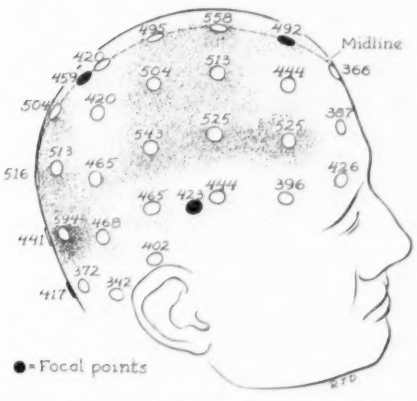


Fig. 2.—Comparison of a 25 cm. and 20 cm. TSD using the Adamson-Kienböck five point method, 100 kv, 300 r. Above, 25 cm. TSD; below, 20 cm. TSD.

fair agreement. With soft radiation, however, such as that employed in our studies (half-value layer, approximately 0.055 mm. of copper or 2 mm. of aluminum), the thimble chamber tends to give slightly lower readings. Nonetheless, our actual determinations of percentage scatter with the thimble chamber on human abdominal skin yielded results which corresponded quite closely with those given by Quimby and colleagues for a Pressdwood phantom using an extrapolation chamber.

The radiation was delivered from a General Electric Coolidge tube apparatus, Model KX-10. At 100 kv this tube produces radiation having a half-value layer of 1.6 mm. of aluminum. This quality radiation was used throughout without filters. Conventionally, the quality of radiations used in the Adamson-Kienböck technique is in the range of 60 to 100 kv. Within this range the penetrations of the x-ray beam are sufficiently similar to be considered equal from a clinical standpoint. About 65% of radiation of this quality reaches a 3 mm. depth, the approximate depth of the hair bulbs which contain the radiosensitive cells ultimately affected by the radiation. Practical experience has not demonstrated the value of added filtration. The other factors used were 10 ma. and target-skin distances of 20 and 25 cm.

For radiation of the above quality it has been shown that the scatter and hence the skin or surface dose is almost independent of the target-skin distance. The scatter increases with the size of the field irradiated, approaching a maximum when the field size reaches 100 to 200 sq. cm. All our measurements were made over unshielded areas with the field sizes determined by the shape of the skull, thus, the field size generally exceeded 200 sq. cm. and could be assumed to yield the maximum scatter. The scatter increases with depth up to a maximum of about 10 cm. with radiation having a half-value layer of about 2 mm. of aluminum. Thus, with the quality of radiation we have employed (1.6 mm. of aluminum), the thickness of the phantom skull is sufficient to give maximal scatter.

It was considered of interest to acquire data bearing on the quantity of radiation actually penetrating the skull into the brain. Accordingly, the ionization chamber was placed inside the skull so that its tip lay directly under the frontal focal point. The paste was then pressed inside the skull so as to occupy all the volume not taken up by the chamber and a 1 cm. layer of paste was placed on the outside of the skull. A single air dose was then administered directly over this focal point using a TSD of 20 cm. and two different voltage factors, 60 and 100 kv. In a correlative study, the spinal fluids of five children who were treated by the Adamson-Kienböck technique employing 400 r to each focal point were collected 24 hours after the irradiation. The cell counts, protein levels, serological tests for syphilis and colloidal gold tests were then determined. All five of these children had experienced postirradiation headaches and severe nausea.

RESULTS

Figure 2 shows the distribution of surface doses with TSD's of 20 and 25 cm. It is at once evident that large portions of the scalp receive doses which are one and one-half to two times as great as that delivered over the focal points. The major region of high dose overlap lies in a more or less solid band about 3 in. wide which runs parallel to the midsagittal line. Its upper boundary is about 1½ in. from the midline and its boundary diminishes anteriorly. The doses within the band are not completely uniform. The actual distribution of this band is shown in Figure 3, a photograph of a 6-year-old boy who was experimentally given a subepilating dose of 200 r in air to each of the five points of the Adamson-Kienböck method. Epilation was essentially restricted to the area of the band where the doses received were adequate for epilation because of overlapping. Correlatively, this would be the area in which permanent alopecia would appear with moderate overdosage. The highest skin dose value occurs in a quite small area about 2 in. from the midline on a level with the occipital focal point. This area receives about two and one-fourth times as much radiation as the air dose of the focal points when the TSD is 25 cm. Thus,

when 300 r in air is given, this spot receives 669 "tissue roentgens." It is apparent from Figure 2 that there is a more even distribution of surface doses when the TSD is 25 cm. rather than 20 cm.

All the values are higher when the TSD is 25 cm. rather than 20 cm. This is due to greater overlapping. In the former case there are four points of radiation on the grid which receive approximately two or more times the air dose radiation delivered

Fig. 3.—Photograph of a patient who was given a subepilating dose of 200 r by the Adamson-Kienböck technique. Epilation approaches completeness only in the overlap areas receiving the greatest quantity of radiation (compare with Fig. 2).

to the focal points. These points lie along the upper posterior margin of the overlap band. When the TSD is 20 cm. only the lateral occipital point mentioned above receives a dose of this order. This point receives with either of these TSD values the single greatest dose. The table shows the skin doses for all the points on the grid when 100 r is administered in air to each of the five focal points.

It is noteworthy that no area of the scalp receives a surface dose less than that of the dose in air given to the focal points. In general the points of low dosage lie along the hair-line in regions where overlapping is minimal. The two lowest values

are in the midsagittal line anteriorly just about at the hair line and in an area which would correspond approximately to the mastoid process. When the TSD is 20 cm., the lowest point receives 114% of the air dose of the focal point and with a TSD of 25 cm. the dose of the lowest point is 124% of the air dose.

Figure 4 shows the distribution of doses when 300 r in air is given to the parietal focal point in the Adamson-Kienböck method. The point directly under the target receives 357 r when the TSD is 20 cm. and 345 r when the TSD is 25 cm. For the 20 cm. TSD, the scatter is 357 —300 = 57. The percentage scatter is thus 57/300

Total Skin Doses Received at Numbered Points on the Grid When 100 r in Air is Administered to Each of Five Points in the Adamson-Kienböck Technique

Points	Target-Skin Distances	
	20 Cm.	25 Cm.
1	122	124
2	129	150
3	142	163
4	148	192
5	175	170
6	132	134
7	186	194
8	171	193
9	175	191
10	148	156
11	165	174
12	168	204*
13	181	181
14	155	152
15	134	141
16	140	180
17	140	196*
18	155	178
19	156	184
20	144	159
21	168	173
22	171	199*
23	198*	223*
24	124	174
25	172	182
26	147	162
Frontal	164	169
Vertex	153	181
Occiput	139	165
Parietal	141	150

* The points receiving approximately 2 or more times the radiation in air given to the centering points.

× 100, or 19%. The percentage scatter is 15% when the TSD is 25 cm. This difference is probably not significant, as it lies within the normal range of variation inherent in the technique of measurement. The measurements were repeated many times over various focal points and the percentage scatter was found to be between 15 and 20% irrespective of the TSD. With the Pressdwood phantom, Quimby and co-workers found that the percentage scatter for radiation having a quality similar to that employed by us was about 28% with a 100 sq. cm. field and a depth giving maximum back-scatter. Our values for percentage scatter over the scalp phantom were thus lower than that recorded for the Pressdwood phantom. This is attributable to the diminished scattering power of bone as compared with soft tissue. When the thimble was placed over the abdominal wall, the percentage back-scatter was found

to be 25 to 30, values which agree with those given by Quimby and co-authors. Over the tibia, however, the back scatter was only 12 to 15%. There is less soft tissue over the tibia than over the calvarium, and, hence, less scatter is to be expected.

In comparing the distribution of doses when a single area is irradiated at TSD's of 20 and 25 cm., it can be seen that the quantity of radiation is approximately similar within a 2 in. radius of the focal point. Beyond this the quantity falls off

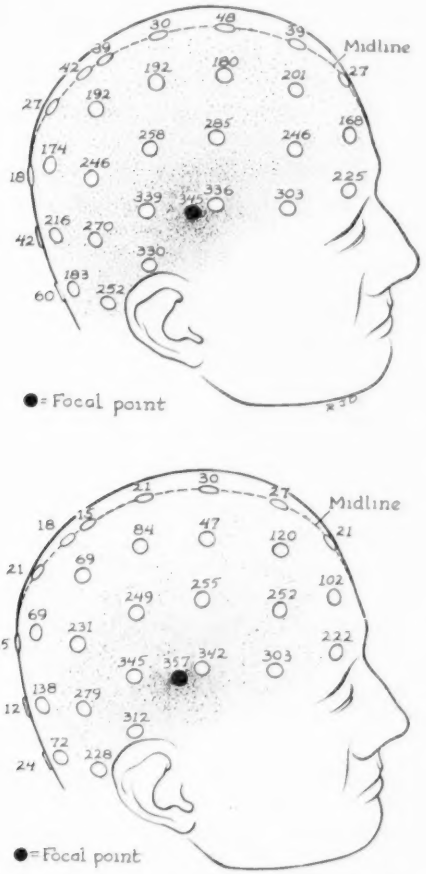


Fig. 4.—Comparison of a 25 cm. and 20 cm. TSD when radiation is given to the parietal focal point. 100 kv, 300 r; above, 25 cm. TSD; below 20 cm. TSD.

rapidly in the case of the 20 cm. TSD. This, of course, accounts for the less even distribution when this TSD is used in the five point Adamson-Kienböck technique. It also explains why the highest skin dose values with the 20 cm. TSD are always lower than those with a TSD of 25 cm.

Other workers who have considered the problem of overlap often speak about areas of double and triple overlap. This may be misleading unless it can be shown that the highest skin values necessarily occur in the areas which receive overlap from

the greatest number of centering points. In order to clarify this we have marked out on the phantom the approximate boundaries of the areas which receive radiation from each of the five focal points. This is done by establishing the points furthest away from each of the focal points which received at least 10% of the air dose. It was necessary to select some arbitrary boundary line, since it was found experimentally that when 100 r in air was given to any focal point the thimble chamber recorded at least a few roentgens when it was placed anywhere else on the scalp. The areas receiving overlap within the 10% boundaries from one or more focal points have been diagramed in Figure 5. There is a small wedge-shaped area roughly between the occipital and parietal regions which receives some of the radiation delivered to each of four focal points. This would then be a quadruple overlap area. Only a small area approximately 3 in. (7.6 cm.) anterior to the upper ear lobe, which would probably correspond to the lateral forehead region, receives radiation

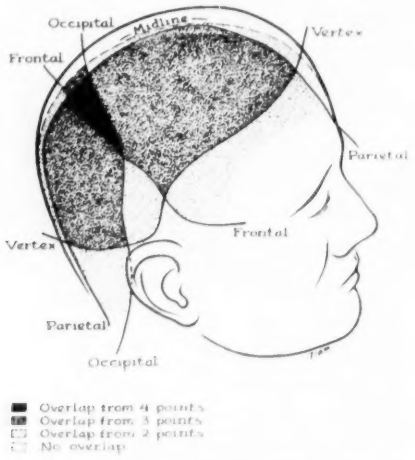


Fig. 5.—Diagrammatic representation of overlap using the standard Adamson-Kienböck technique. The boundary for each focal point is the area receiving 10% of the air-dose given to the focal point.

from a single focal point. One must appreciate that the overlapping shown in this sketch has no meaning quantitatively; that is, the quadruple overlap area is not the region which actually receives the greatest quantity of radiation. It is simply the area which has received at least 10% of the radiation delivered from each of four points. Actually the greatest portion of the scalp receives some overlap from three centering points.

When the ionization chamber was placed inside the skull and the radiation delivered to the phantom directly over the tip of the chamber, it was found that with 100 kv at a 20 cm. TSD 25% of the radiation had penetrated the calvarium. With 60 kv this value was 14%. The spinal fluid of five patients with severe postirradiation reactions did not show abnormalities in cell count, protein content, serologic tests for syphilis or the colloidal gold curve. The meningeal reaction was thus minimal or occurred at some time other than when the tests were made.

COMMENT

The estimates of previous investigators that some areas receive twice as much radiation as the focal points have been confirmed. In fact, there is a small area over the occiput which receives two and one-fourth times as much radiation as the air dose over the focal points with a 25 cm. TSD. Although the distribution of the absorbed radiation is uneven, there are fairly large scalp areas which receive one and one-half to one and three-fourths times more radiation than the focal points. From the practical standpoint, the important question is whether the higher quantity of radiation in the zones of overlap approaches the permanent alopecia dose. Unfortunately, this latter dose is not known, although it must be considerably higher than earlier estimates. When 400 r in air is given to each focal point, the highest skin dose value will be 900 r when the TSD is 25 cm. On a few occasions we have experimentally administered 500 r to each of five focal points at a TSD of 25 cm. In these cases, approximately 1,125 r is absorbed by the skin in the region of highest dose. The permanent alopecia dose apparently exceeds 1,000 "tissue roentgens." It is obvious, however, that one cannot determine either the permanent alopecia dose or the minimal (threshold) epilation dose by using the Adamson-Kienböck technique or any other technique in which overlapping is an intrinsic feature. To do this, the test area must be irradiated from a single source. Some of our preliminary studies bear on this. For instance, although it is frequently asserted that 300 r in air constitutes an epilating dose, this may be misleading unless qualified. It is true only when this dose is given to each of five unshielded focal points. We have determined that in children 4 to 8 years of age, 300 r in air frequently does not produce a complete defluvium within a 3 cm. wide circle directly under the target (100 kv, TSD 25 cm.). Our preliminary data indicate that the minimal epilating range for many children is 350 to 400 r in air when the observations are made five to six weeks after irradiation. Assuming the percentage scatter to be 20%, this represents 420 to 480 "tissue roentgens." Three hundred roentgens in air is an adequate epilating dose when administered by the Adamson-Kienböck technique chiefly because overlapping insures higher doses all over the scalp.

MacKee and Cipollaro advocate 300 r as the dose which should be used in the Adamson-Kienböck technique. Others consider this dose to be inadequate and employ 400 to 425 r. In our experience, an imperfect defluvium occasionally results with 300 r. In such cases it is particularly the hair along the hair line, especially in the frontal area, which fails to epilate. Our present data show that these are the very areas which receive the lowest quantity of radiation. If about 350 to 400 r in air (approximately 420 to 480 r in tissue) is the minimal epilating dose for many children, then Figure 2 shows that the skin doses along the hair-line areas are quite close to or below the minimal epilating dose. In these areas a number of factors, such as improper positioning of the head, unusually shaped heads, or slight movements, can cause the dose to fall below the threshold epilation level. For these reasons we routinely give 400 r in air (Adamson-Kienböck technique) except to 2 to 3-year-old children with small heads (350 r in air is given instead). The results have been excellent in over 200 cases save for one instance in which even 400 r did not cause a complete epilation. No irregularities were observed in four cases which received 500 r in air except for a possible slight increase in the time required for hair regrowth. Our views sharply disagree with those of Lane and Crawford, who

consider that doses of 280 r in air give satisfactory results in children and that complete epilation is not necessary for therapeutic success. Undoubtedly many cases can be "cured" with inadequate epilation. This might be because the disease may not involve the unepilated areas. Also, an additional two months or more are required after the irradiation before there is initial regrowth of hair and many months before the hair is restored to its original length. Spontaneous cure can occur during this time. We have observed this.

A review of the available data yields nothing which would weaken the widely held belief of experienced persons that the Adamson-Kienböck method is safe and efficient for the treatment of tinea capitis. There must be a large difference between the smallest dose which will cause epilation and the largest dose which will just fail to prevent the regrowth of hair. This figure is not precisely known at present, but it is great enough to insure the safety of this method. Pendergrass and Mahoney have rejected the Adamson-Kienböck technique because of the dangers which they suppose to be inherent in the phenomenon of overlapping. They give 500 r in air to each of five carefully shielded areas. We have found this method difficult, arduous, and time-consuming. Because of difficulties in critical shielding, not infrequently narrow strips will receive little or no radiation or will be exposed twice and thus receive considerably more than 500 r. The latter error has no untoward consequence; the former may leave infected hairs unepilated.

The Adamson-Kienböck technique has been in use for half a century. There is no clearcut evidence that, when properly performed, such irradiation has caused later neurologic or cutaneous complications. Still, it is a matter of note that with x-rays delivered at 100 kv at least 25% of the radiation measured in air penetrates the calvarium. Meldolesi found an increase in spinal fluid albumin and glucose following scalp irradiation. He considers that this reflects circulatory changes in the cerebrum and advises that in order to prevent brain damage one should combine thallium acetate therapy (4 mg. per kg.) with half the usual dose of x-rays.

The habit of referring to the intermediate areas between centering points as double or triple overlap areas should be given up. The area receiving overlap from the greatest number of ports does not correspond to the area receiving the highest quantity of radiation. Moreover the quantitative variations in the dose are very great within the triple overlap area. Twenty-five and not 20 cm. is the preferred TSD, even though the radiation time is considerably less with the latter. With 20 cm. there is less overlap, the dosage distribution is less uniform, and, most important, some areas may remain unepilated when the circumference of the child's scalp exceeds 20.5 cm.

Finally, none of the qualitative figures presented for the dosage distribution when the Adamson-Kienböck method is used should be considered to have absolute or precise value. Heads vary markedly in size and shape. Accordingly, the figures will be different for each scalp.

SUMMARY

We plotted the radiation received in the skin over various portions of the scalp when superficial x-rays were given by the Adamson-Kienböck technique. A small area of overlap was observed on both sides of the occipital midline which receives in

"tissue roentgens" over twice the air dose administered to the focal points. Most of the scalp receives doses which are one and one-half times or more than the air dose administered to a focal point.

The radiation is distributed with greater uniformity when the target-skin distance (TSD) is 25 cm. rather than 20 cm. The radiation delivered to a single point falls off less rapidly at the periphery when a TSD of 25 cm. is used instead of a TSD of 20 cm. Preliminary studies indicate that the minimal, or threshold, dose for temporary epilation exceeds 300 r in air. The data support the belief, validated by clinical experience, that the Adamson-Kienböck technique is quite safe for the routine epilation of fungus-infected scalps, provided that it is done by experienced personnel with well-calibrated equipment.

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DERMATOLOGIC MANIFESTATIONS OF MONGOLISM

ISRAEL ZELIGMAN, M.D., Med. Sc.D.
BALTIMORE
AND
SAMUEL P. SCALIA, M.D.
PIKESVILLE, MD.

THE INCIDENCE of Mongolism is greater than is commonly realized. Beidleman reported 3.4 Mongoloid births per 1,000 births at the Lying-in Hospital in Boston. Benda estimated that in 1943 there were at least 60,000 Mongoloid persons in the United States.

The term "Mongolism" used for these patients refers to their superficial resemblance, at an early age, to the Mongolian race. Benda believes that Mongolism is the opposite of acromegaly and hence is due to hypopituitarism, but not all authorities accept this theory.

The Mongoloid person has certain physical deviations which distinguish him in appearance from normal persons, yet these same defects make all Mongoloids resemble each other. These characteristics are not a result of mental deficiency, but are evidence of an actual essential growth disorder involving the entire skeletal system.

Among the major deviations is that of the skull, which in Mongoloids is rounded, so that the anteroposterior diameter tends to equal the transverse diameter. A large forehead results, so that the face looks short. The anterior fontanelle is large and is slow in closing, and the skull sutures often remain un-united throughout childhood.

The formation of the eyes is a most conspicuous anomaly. The Mongoloid has short, slanting palpebral fissures which slant upward toward the lateral edge. At the medial corner, the angle is covered by a skin fold, the "epicanthus." As mongoloids get older, this feature tends to disappear. Malformations of the iris and lens, and abnormal ocular movements are also frequent.

There are anomalies of the external ears and of the nose. The voice has a characteristic rasping low pitch, regardless of age. The nasal septum is frequently encrusted and rhinorrhea is very common and often associated with abnormal sinus formation.

Dentition in the Mongoloid child is abnormal. The first dentition is usually greatly delayed, and second dentition is irregular and frequently never takes place. There is abnormal alignment, general hypoplasia of teeth, gingivitis, and conspicuous absence of caries despite poor dental hygiene.

The abdomen is distended and umbilical hernias are frequent. The male sex organs are retarded in development and there is cryptorchism in 50% of males. In females, the menarche is late and menopause quite early.

From the Rosewood State Training School, Owings Mills, Md.

The extremities are short, especially the hands, fingers, feet, and the toes. The terminal phalanx of the little finger is usually rudimentary and curved toward the midline, and the thumb is short resulting in a "spade-like" hand.

The heart in Mongoloids tends to have congenital septal defects as well as other anomalies.

Mongoloid children have a stunted growth or a type of dwarfism. Mentally, the Mongoloid is usually an imbecile. There are many other abnormalities, but these are some of the major features.

DERMATOLOGICAL MANIFESTATIONS

At Rosewood State Training School, there were at the time of our investigation 1,458 inmates, all white. Of these, 106 were Mongoloids. Since very little informa-

Dermatologic Manifestations in Mongoloid Patients

Total patients with Mongolism	106
Protruding and/or fissured lower lip	106
Scrotal or enlarged tongue	101
Acrocyanosis	91
Increased number of creases on palms and soles	79
Xerosis or ichthyosis	73
Keratosis palmaris et plantaris	22
Actinic sequellae—lentigines and atrophy	15
Acne vulgaris	5
Rosacea	5
Blepharitis	3
Sebaceous cysts	3
Seborrheic dermatitis	3
Pyoderma	3
Vitiligo	3
Alopecia areata	2
Onchomycosis	2
Histiocytoma	2
Verruca vulgaris	2
Onychia	2
Alopecia totalis	1
Atopic dermatitis	1
Callositas, multiple	1
Carotenemia	1
Folliculitis	1
Herpes simplex	1
Keratosis pilaris, extensive	1
Psoriasis	1
Senile keratosis	1
Tinea pedis et manis	1
Tinea versicolor	1

tion concerning cutaneous traits of Mongolism was available, a study was initiated with a view to a statistical analysis of the dermatological manifestations of this group of individuals. Their ages varied from 1 to 43 years. There were 62 males and 44 females. All the patients were white and of varied ethnic groups. Seven had active pulmonary tuberculosis.

Several features were noted quite commonly in these patients. One hundred six had a protruding and/or fissured lower lip. A scrotal or enlarged tongue was seen in 101 instances. Acrocyanosis was noted in 91 patients. The number of creases on the palms and soles was noticeably increased in 79 subjects. Seventy-three of these Mongoloid patients had either xerosis or frank ichthyosis, while 22 manifested keratosis palmaris et plantaris. Lentigines and skin atrophy of exposed parts were seen in 15 of the older Mongoloids (aged 17 to 42).

In addition, there were scattered cases of acne vulgaris, rosacea, blepharitis, sebaceous cysts, seborrheic dermatitis, pyoderma, vitiligo, alopecia areata, onychomycosis, histiocytoma, verruca vulgaris, and onychia. Individual cases were seen

of alopecia totalis, atopic dermatitis, callositas, carotenemia, folliculitis, herpes simplex, keratosis pilaris, psoriasis, senile keratosis, tinea pedis et manis, and tinea versicolor (Table).

COMMENT

Relatively little attention has been paid to the cutaneous disorders manifested by Mongoloids. Benda mentioned the fissuring and dryness of the lips and the scrotal tongue. He stated that protrusion of the tongue was due to the smallness of the oral cavity rather than to the increased size of the tongue.

He also noted that the skin of the Mongoloid baby is soft, thin, and velvety, and that the trunk and thigh appear marmorated because the capillaries are marked and congested. When the Mongoloid grows older, he found that the skin becomes thick, dry, and rough. He also stated that the skin of Mongoloids is "susceptible to eczema." Increased wrinkling of the palms and soles was noted by him.

Our survey corroborated the fissuring of the lips, the frequent presence of scrotal tongue, the acrocyanosis, and the xerosis of the older mongoloids, as well as the increased number of creases or wrinkles on palms and soles. The keratosis palmaris et plantaris and the actinic sequellae paralleled the increased dryness of the skin of the older Mongoloids. The other cutaneous manifestations noted were not greater than normal individuals might have shown. No greater tendency to eczematous eruptions was seen.

SUMMARY

A survey was undertaken of the dermatologic manifestations of Mongoloid patients at the Rosewood State Training School.

Frequent cutaneous findings were: protruding and/or fissured lower lip, scrotal or enlarged tongue, acrocyanosis, increased number of creases on palms and soles, xerosis or ichthyosis, keratosis palmaris et plantaris and actinic sequellae.

Other skin disorders appeared not to exceed the expected norm, and there was no evidence of a marked tendency on the part of Mongoloids to develop eczematous eruptions.

1109 N. Calvert St. (2)

1004 Reisterstown Rd. (8)

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URTICARIA PIGMENTOSA APPEARING AS A SOLITARY NODULAR LESION

LOUIS CHARGIN, M.D.
AND
PERRY M. SACHS, M.D.
NEW YORK

URTICARIA pigmentosa, although a relatively uncommon clinical entity, is nevertheless a well established and well recorded affection in its three forms. An analysis of reported cases shows that the majority, 65%, are of the macular variety, 25% of the mixed or maculonodular type, while 10% represents the purely nodular type.

In all forms, the affection, characteristically, appears as widespread numerous lesions, and while the number may vary, cases showing few lesions are quite uncommon. Indeed, the literature cites only a few examples with few lesions and still fewer with just a single lesion. Little refers to a patient whose eruption was limited to two lesions. Gross and Novy each presented a case with a single nodule of urticaria pigmentosa, and recently Scott and Lewis reported another such example.

In the past two years, in conjunction with other dermatologists, we have had the opportunity to study seven cases, all in infants, of urticaria pigmentosa appearing as a single plaque or nodule. Six are cases of other dermatologists, while the seventh is a personal one. They have been observed for a varying length of time, up to three years, thus affording information concerning the nature and course of the affection in this, its limited form.

With this group of cases serving as a basis, it is the purpose of this presentation to discuss the pertinent clinical and microscopic features of this variety of urticaria pigmentosa. Furthermore, we shall consider the important diagnostic points, note the clinical course to date, and comment on the nature of this dermatosis.

REPORT OF CASES

Since the seven cases clinically and microscopically show striking similarity in their main features, it would be repetitious to delineate each.

Case F. N.,* our own, which will serve as a typical example of the group, was a 20-month-old white boy, who presented a round plaque-like infiltration on the left forearm, 2 cm. in diameter, of reddish-brown color and smooth surface (Fig. 1). The lesion appeared at birth, and to date, three years later, has not changed appreciably in size. However, it has tended to flatten and the intensity of the original color has diminished. As far as can be determined, there are no

Read at the meeting of the American Dermatological Association, Lake Placid, N. Y., June 13, 1953.

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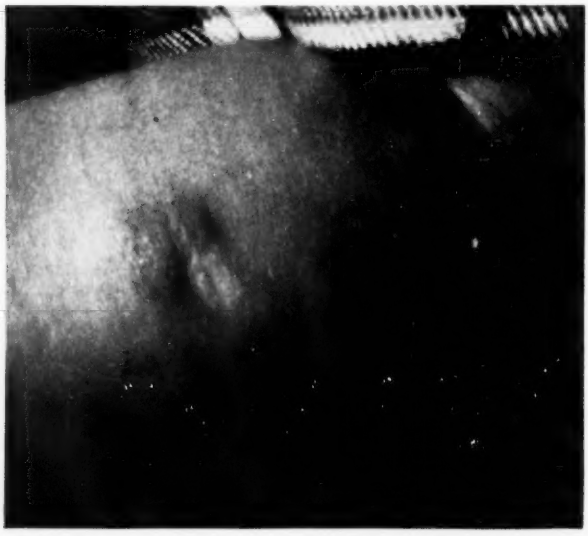

Fig. 1 (Case F. N.).—Nodule of urticaria pigmentosa of forearm.

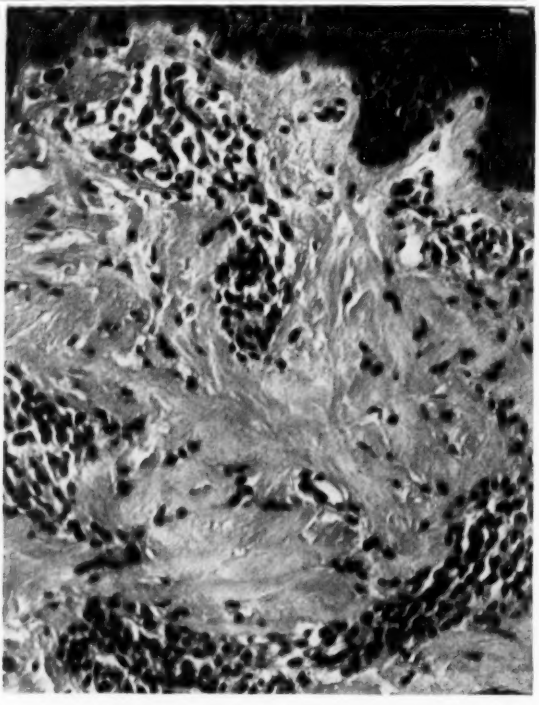

Fig. 2 (Case F. N.).—Nodule of urticaria pigmentosa showing uniform focal mast cell infiltration. Hematoxylin and eosin stain.

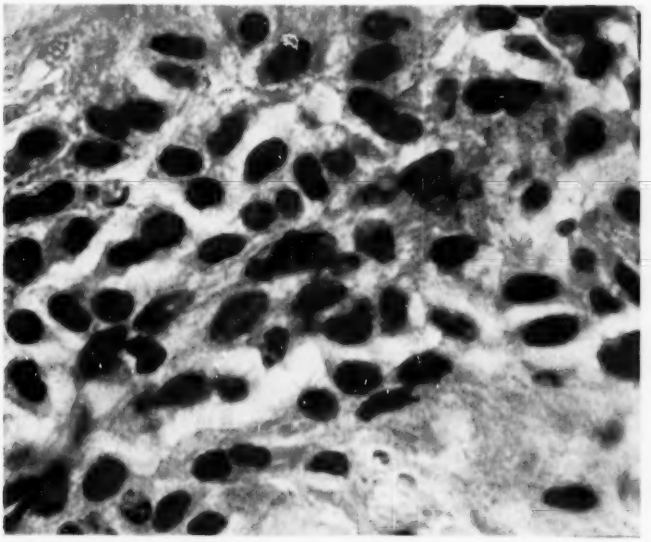

Fig. 3 (Case F. N.).—Nodule of urticaria pigmentosa showing mast cells on routine stain. Hematoxylin and eosin stain.

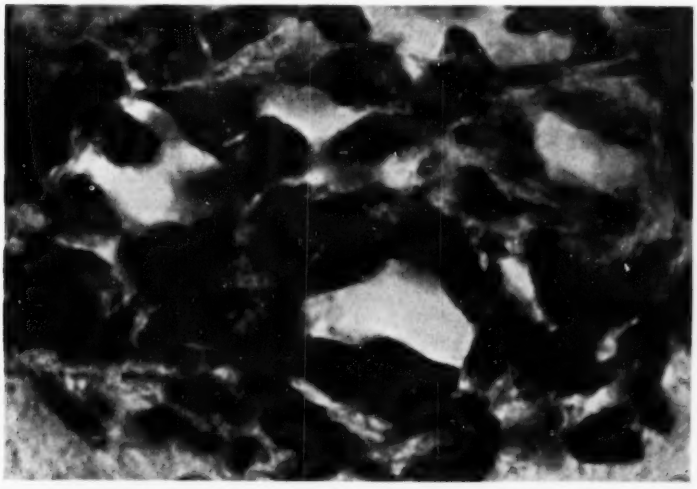

Fig. 4 (Case F. N.).—Nodule of urticaria pigmentosa showing mast cells at high magnification. Polychrome methylene blue stain.

Summary of Cases of Urticaria Pigmentosa Appearing as Single Plaque or Nodule

Doctor	Patient	Sex	No. of Lesions	Age at Onset	Age Biopsy Done	Site	Color	Size	Urticates	Bullae	Family History	Original Clinical Diagnosis
					Cases Observed							
Robinson, M. M.....	C. C.	F	1	3 mo.	6 mo.	Chin	.....	1 cm.	....	....	Neg.	Nevoxanthoma
Greenhill, S.	J. J. M.	M	1	2 wk.	5 mo.	Ankle	Pigmented	4.5 cm.	Yes	Yes	Neg.	Erythema multiforme or bullosum
Noun, M. H.....	M. J.	F	1	2 wk.	2 mo.	Back	.....	.....	....	Yes	....	.....
Satulsky, E. M.....	P. H.	F	1	At birth	19 mo.	Leg	Brown pink	3 cm.	....	Yes	Neg.	Nevus?
Sachs, P. M.....	F. N.	M	1	At birth	20 mo.	Forearm	Red brown	2 cm.	Yes	Yes	Neg.	Nevus
Waldriff, G.	J. B.	M	1	At birth	3 mo.	Wrist	Flesh to pink	2 cm.	....	Yes	Neg.	Nevus or lymphangioma
Kendrick, F.	D. C.	M	1	2 mo.	12 mo.	Side of Chest	Yellow	.....	Yes	....	....	F. b. reaction or xanthoma
Author					Cases Reported in Literature							
Gross, 1933	R. C.	M	1	16 days	.....	Thigh	Brown	2 cm.	Yes	Yes	....	.....
Novy, 1948	W. R.	F	1	At birth	.....	Scapula	Light brown	3 cm.	Yes	Yes	....	.....
Scott and Lewis, 1953	L. N.	M	1	1 mo.	.....	Forearm	Yellow tan	2.3 cm.	Yes	Yes	....	.....

subjective symptoms, since the child does not especially scratch the lesion. Mechanical friction definitely urticated the patch with resulting erythema, and at times caused the formation of a bulla. Recently this bullous response had not occurred. No other member of the family is affected. At first the lesion was thought to be a nevus, the type undetermined; but histologic study identified the true nature of the lesion as a nodule of urticaria pigmentosa.

Microscopically, throughout the upper and mid cutis are dilated blood vessels and a mild interstitial edema. There is a focal and diffuse infiltration composed chiefly of fairly uniform cells, which show a varying amount of cytoplasm and round or oval vesicular nuclei (Figs. 2 and 3). The polychrome methylene blue stain identifies them as mast cells (Fig. 4). The epidermis shows no significant changes. However, there is a moderate amount of pigment in the lower portion, particularly in the palisade margin, which is intact.

CLINICAL FEATURES

The Table, based on a study of 10 cases, 7 of our own, and 3 that are recorded in the literature, summarizes the essential clinical findings. The most prominent clinical feature of these cases is the presence of only a single lesion throughout the entire course of the dermatosis. In accord with this fact, Gross † noted that no new lesions developed in his case in the interim from the destruction of the nodule soon after its appearance in early childhood to 17 years later. Further analysis of the various features shows the following:

Sex.—This plays no significant role. Six were males and four females.

Onset.—The affection appears at birth to three months with the majority occurring between birth and two weeks. Four patients presented the lesion at birth.

Site.—The site of the lesion, for the most part, is on the extremities; three occurred on the lower and three on the upper. Three were on the trunk and one on the chin.

Color.—Information respecting color was obtained in eight of the cases and was given as pigmented, yellowish yellow-tan, pink, brown, red-brown, and flesh to pink color. Thus the color may vary but shows a predilection for some shade of brown with mixture of red and yellow.

Size and Shape.—As a rule the lesions are round or oval, nodular or plaque-like, and in size vary from 1 to 4.5 cm., most being 2 cm.

Urtication.—Since urtication is a familiar and important feature of urticaria pigmentosa, it was naturally inquired into closely. However, we were able to obtain this information in only six of the cases. All of these showed this feature which was elicited by mild trauma or stroking. Spontaneous and pronounced itching was a feature in some of the cases as evidenced by scratching. This tendency diminished with time.

Bullae.—In 7 of the 10 cases, we were able to obtain data regarding this feature and it occurred in all seven. We have learned to regard this bullous formation as a most important feature of this type of urticaria pigmentosa; indeed, it is of diagnostic importance. This vesicle or bullous response occurred following slight trauma or minor irritation and possibly in some of the cases spontaneously. The bullae tend to recur and are superimposed on the nodule (Fig. 5). They are of short duration, and the ruptured bullae release a clear colorless fluid.

Course.—From observation of our cases, it is impossible to express a definite opinion except to state that in none has the lesion disappeared, some having been

† Personal communication to the authors.

followed as long as three years. Novy ‡ states that his patient, reexamined five years after first observation, showed slight increase in size of the lesion and continuation of urtication and vesiculation on slight trauma. However, the color has faded to some degree, and the pruritus has diminished. Satulsky's case, seen 19 months after the initial examination, showed some involution and a decrease in pigment. In Sachs's case, which was followed for three years, the lesion became flatter and the color diminished.

Thus, it can be stated that the affection which appears as a single lesion remains so throughout its course, and that no generalization takes place. It is to be noted that the lesions do not remain stationary, but show a tendency to undergo change in size, color, etc., perhaps to eventual spontaneous disappearance.

Fig. 5 (Case J. B.).—Nodule of urticaria pigmentosa showing vesiculation on dorsum of hand.

CLINICAL DIAGNOSIS

The paucity of cases reported of a single lesion in urticaria pigmentosa hardly represents the actual incidence. We feel that cases of this type are far more common than the literature indicates, and have been unrecognized or misdiagnosed. Probably, in most instances, pigmented cellular nevus and xanthoma or nevoxanthoendothelioma were the diagnoses chiefly considered for this dermatosis.

It may be difficult to differentiate clinically the single nodule of urticaria pigmentosa from a cellular pigmented nevus, since the color and the general appearance, namely, that of a slightly raised nodule or plaque, is common to the two. Likewise, the nodule of urticaria pigmentosa and that of xanthoma or nevoxanthoendothelioma may manifest a similar yellow or red-yellow color. However, the constant characteristic findings of urtication and vesiculation, derived from the history or

‡ Personal Communication to the authors.

seen or elicited upon examination, readily distinguishes the urticaria pigmentosa nodule from the other lesions. Microscopic study offers further conclusive evidence, since these entities have their distinct pictures.

It is also significant to note that the vesicular feature of this affection may cause error in diagnosis prior to microscopic study, mistakes being in the direction of lymphangioma or some bullous form of eruption.

In summary, it may be stated that this dermatosis should be suspected, clinically, if a solitary lesion, disregarding site, of nodular or plaque-like nature, is encountered at birth or soon thereafter. The color is a shade of brown with varying intensities of yellow and red. The urticarial and vesicular response to trauma establishes the diagnosis.

MICROSCOPIC FEATURES

It is noteworthy that in all cases, including those reported in the literature, the microscopic findings are strikingly alike. In fact, there is little and only minor variation in the microscopic pictures of this group.

In all the cellular infiltration is decidedly pronounced, and the cells, while at the onset focal about the vessels, almost always are diffuse throughout most of the cutis. The cells are fairly large (at least two or three times larger than a small round cell) and uniform, with definite cytoplasm. The nuclei are large, for the most part oval-shaped and vesicular. When stained with polychrome methylene blue, they prove to be mast cells.

In most instances the epidermis shows no significant changes. In almost all of the sections are small areas wherein the basal cells are washed out. In one case there is a moderate concentration of pigment in the lower epidermis, while in another there is only a small amount. The rest are free of any epidermic pigment.

In one of the three cases showing bullous formation microscopically, a large subcorneal bulla, containing polymorphonuclear leukocytes, is seen. Another case shows a similar picture, but the bulla is smaller and is associated with a small ulceration. This bullous lesion, however, is not entirely subcorneal but penetrates deeper into the epidermis. In the sections of the third case the vesicle is again intraepidermic; however, most of the epidermis is missing and the surface is crusted, containing numerous polymorphonuclear leukocytes. Thus it can be stated that the vesicles are located in the epidermis, particularly in the upper portion.

MICROSCOPIC DIAGNOSIS

The microscopic features, namely, the morphology of the cells and the uniformity of the infiltration are indicative of nodular urticaria pigmentosa. This diagnosis is established on sections stained routinely and corroborated by special stain, which proves the presence of mast cells.

It is pertinent to stress that the type of cell seen in urticaria pigmentosa characterized by a single lesion is the same as that in the nodular type with numerous lesions (Figs. 6 and 7). Furthermore, it should be noted that the mast cell of the nodular type of urticaria pigmentosa differs in appearance from the mast cell in the macular or the maculopapular type. While in the nodular type the infiltration suggests that of a possible nevus or a lymphoblastoma, in the macular type the cell resembles a wandering connective tissue cell, such as that seen in a superficial inflammatory process. In the latter the cells are more oval, smaller, and consist chiefly of a nucleus.

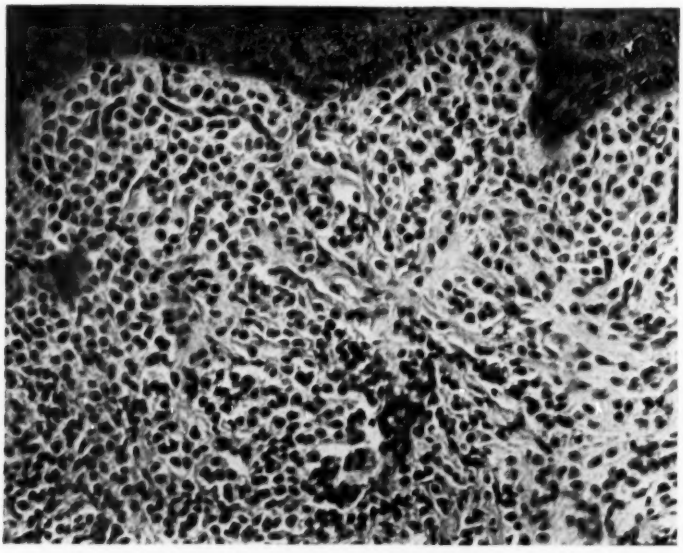

Fig. 6 (Case C. C.).—Nodule of urticaria pigmentosa showing uniform diffuse cellular infiltration. Hematoxylin and eosin stain.

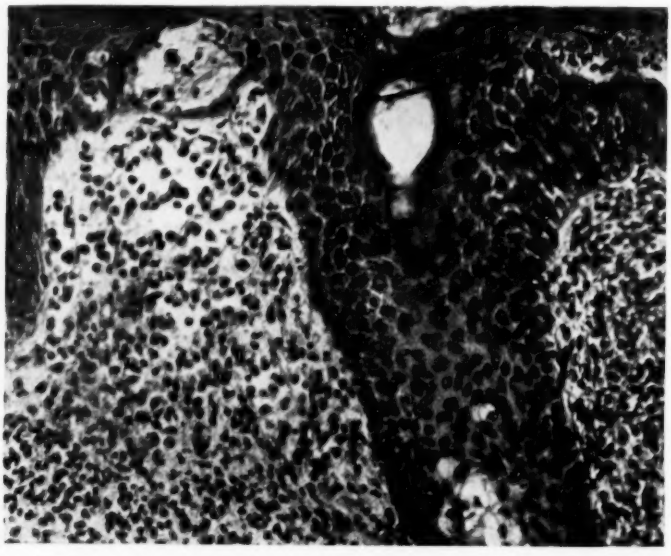

Fig. 7.—Nodule of urticaria pigmentosa from a case of multiple lesions showing a picture similar to Fig. 6, a case of one lesion. There is evidence of an intraepidermic vesicle. Hematoxylin and eosin stain.

Microscopically, this condition although diagnostic, because of the uniform intense cellular infiltration must be differentiated from a lymphoblastoma, particularly mycosis fungoides in the tumor stage. However, the absence of Pautrier's abscesses, the decided uniformity of the cells, the fact that they are mast cells, and lastly, that the source of the biopsy is an infant, conclude against such a diagnosis.

The microscopic picture, also, gives the impression of an intradermic cellular nevus, mainly due to the relative absence of inflammatory cells, and the fact that the appearance of the individual cell is not unlike a nevus cell. However, this possibility is ruled out by the distinct uniformity of the cells and proof that they are mast cells. In addition, there is an absence of multinucleated cells and intracellular pigment, as well as a lack of the characteristic grouping and arrangement, which are features of an intradermic nevus.

Although clinically the lesion resembles xanthoma or a lesion of a nevoxanthoendothelioma, the absence of foam cells and Touton cells and the presence of mast cells offer a basis for adequate microscopic differentiation.

NATURE OF THE DERMATOSIS

Clinically, as well as microscopically, this affection presents features of a nevus or nevoid process. This applies to urticaria pigmentosa as a whole, but particularly to the type under consideration. This is not original, but has been expressed by many, including Unna, Jadassohn, Noble, Bloch, Little, Török, and others. Dissenting opinions are comparatively few and these, for the most part, consider the process to be inflammatory in nature.

Török has adequately discussed the points in favor of the nevus concept. Briefly stated, they are "inborn anlage," appearance of lesions in early life or at birth, the familial nature, in most instances, persistence of the affection with little change, and clinical similarity of the lesions to nevi. Also, while mast cells are typical for urticaria pigmentosa, they occasionally may be seen in nevi. Furthermore, it is not unusual for nevi to appear in later life, a manifestation also true of urticaria pigmentosa. However, Török notes in disagreement the preponderance of mast cells in urticaria pigmentosa, the recurrent episodes, and urtication. We may add, on the basis of our experience, vesiculation.

We feel that the findings in our series of cases favor and tend to substantiate the view that urticaria pigmentosa is a nevus. In accord, several of our patients had the lesion at birth and some of the cases clinically resembled pigmented nevi. Also, to counter the argument that urticaria pigmentosa presents many lesions in contrast to a nevus, our cases feature one lesion.

SUMMARY

Ten cases, including three in the literature, of urticaria pigmentosa, each appearing in the form of a single lesion, are discussed.

The affection appears in infants either at birth or soon thereafter.

The lesion is a nodule or plaque, averaging 2 cm. in size, the color of which shows shades of brown, red, and yellow.

Urtication and vesiculation, following minor trauma and perhaps occurring spontaneously, are diagnostic features of this type of urticaria pigmentosa.

Microscopically, the findings are characteristic, diagnostic, and identical with those in the nodular form of urticaria pigmentosa with multiple lesions.

The entity is apparently more common than the literature indicates; only three prior cases have been reported.

The affection is to be differentiated chiefly from pigmented nevus, xanthoma, and nevoxanthoendothelioma.

Clinically and microscopically the affection resembles a nevus or a nevoid process.

Cases of the following dermatologists are included in this report: Robinson, M. M.; Greenhill, S.; Noun, M. H.; Satulsky, E. M.; Waldriff, G., and Kendrick, F.

1 W. 85th St.

55 E. 86th St.

ABSTRACT OF DISCUSSION

Dr. Carl W. Laymon, Minneapolis: Dr. Chargin has adequately and concisely summarized the clinical and histologic features of the unusual, solitary, nodular type of urticaria pigmentosa. Even now, as he indicated, the pathogenesis of the disorder is far from clear. Actually we know little concerning its etiology and, as a rule, we cannot influence it by treatment.

The disease is a difficult one to classify. Dr. Chargin felt that the cases which he studied were most likely nevi, using the term in a broad sense. There are several features, however, which make its classification with nevoid malformations, especially nevus pigmentosus, unsatisfactory. The same remarks apply to its alignment with ordinary urticaria.

There are several features which strongly suggest that urticaria pigmentosa may be a systemic disorder rather than a purely cutaneous one.

First, osseous lesions associated with urticaria pigmentosa were described by Sagher and shortly thereafter by Clyman and Rein. Of nine cases which were adequately studied, three showed osseous abnormalities of various types which suggested osteoporosis, bone infarct, metastatic carcinoma, or osteochondroma. Sagher claimed that, in his case, the osseous lesions were in the regions of cutaneous involvement. Histologic studies of the bones in these cases would be extremely valuable. Perhaps the bizarre findings represent osseous mastocytomas. One might hypothesize that this disorder may be mastocytic granuloma of bone and skin comparable to eosinophilic granuloma of bone with cutaneous lesions.

Second, hematologic changes in urticaria pigmentosa have been reported and may be of some significance. Among these are prolonged bleeding and clotting times, anemia, and low prothrombin and erythrocyte levels. Some French authors regard urticaria pigmentosa as a type of pseudoleukemia. From material which I reviewed I believe that it is impossible to align urticaria pigmentosa with leukemic disease.

Third, which is perhaps most important, is the relationship between the mast cell and the elaboration of the anticoagulant heparin. This relationship has been demonstrated again and again. It is well known that urticaria pigmentosa is characterized histologically by a mast-cell infiltrate which is sometimes so outspoken that we can regard it as a mast-cell tumor or mastocytoma. Thus, there is obviously a linkage between urticaria pigmentosa and heparin.

Konrad and Winkler of Innsbruck recently performed interesting experiments on a case of extensive, bullous urticaria pigmentosa. Many mast cells were found in the fluid from the bullae and it could be shown that the fluid had a strong anticoagulant effect. This probably explains the purpura which sometimes occurs around ordinary lesions of urticaria pigmentosa. Moreover, their patient showed a noticeable hypersensitivity on intracutaneous testing with heparin. The intracutaneous injection into an ordinary lesion caused the formation of a bulla. Similar though less intense reactions developed on normal skin.

Thus, in urticaria pigmentosa there is a definite hypersensitivity to the products of mast cells. It would be interesting to perform similar experiments on the bullae which Dr. Chargin found in his patients with solitary nodules.

I should like to thank Dr. Chargin for the privilege of discussing his excellent paper.

Dr. Louis H. Winer, Beverly Hills, Calif.: We have been doing cytologic spreads, not only on the bullous type, but also on the generalized type, and we are able to show mast cells in our smears, as Dr. Laymon has indicated.

DR. LOUIS CHARGIN, New York: I thank Dr. Laymon for his valuable and interesting remarks covering the newer findings in the general topic of urticaria pigmentosa, but, as stated in my opening remarks, Dr. Sachs and I have purposely refrained from going into these phases of urticaria pigmentosa because we felt that they are not germane to the subject of our presentation. It was our intention at this time merely to call attention to a form of urticaria pigmentosa that seems to have escaped the notice of clinicians. Again I wish to stress that the condition is diagnosed with ease when one bears in mind the few essential points, namely, a nevus-like lesion appearing at birth or soon thereafter; that this lesion is single, and that it urticates and vesicates on even mild trauma, features not observed in the type of nevus that comes into question and with which this condition can be confused.

We have not studied the fluid contents of the vesicles and cannot express an opinion regarding the interesting observation of Dr. Winer. It may prove to be an additional diagnostic aid in these cases.

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ADULT PREMENSTRUAL ACNE

An Entity Suggesting Corpus Luteum Dysfunction

BEN A. NEWMAN, M.D.
AND
FRED F. FELDMAN, M.D.
BEVERLY HILLS, CALIF.

THE PILOSEBACEOUS structures apparently can be stimulated by a variety of substances, resulting in either acne vulgaris or acneform eruptions. Examples of diverse etiologic types of acne are borne out by tropical acne and chloracne. Bromides, iodides, and certain foods are known to produce acne in some patients or aggravate a previously existing eruption. Emotional factors and foci of infection may play a causal or contributory role. Acne has occurred following corticotropin (ACTH) and cortisone therapy and with adrenal and anterior pituitary tumors. Accumulating evidence points to the endocrine system as playing an important role in the pathogenesis of acne vulgaris. In recent years an excess of androgens, or a deficiency of estrogens, or varying the ratios between androgens and estrogens have received most emphasis as the major etiologic factors of adolescent acne. Most reports in the literature on the hormonal aspects of acne have dealt with the administration of estrogens. In spite of many favorable reports it is not generally accepted that uniformly good results are obtained by the use of estrogens in acne patients. In our experience the results of the use of estrogenic hormones alone have been disappointing. Other hormonal agents that have been used with varying success include thyroid, progesterone, testosterone, pregnant-mare serum, chorionic gonadotropin, and prolactin. The multiple etiologic factors involved in acne and the complexities of the endocrinologic aspects probably account for the frequent failures of hormonal therapy. Lack of individualization of treatment and/or lack of careful definition of the clinical varieties of acne may also be responsible.

As a result of our study of a group of adult female patients with recalcitrant acne which presented a characteristic clinical picture and a specific response to progesterone, we feel that we have differentiated a clinical variety of acne of a specific endocrinologic type. The features of the clinical picture to be described are probably familiar to most dermatologists. However, to our knowledge, the delineation of this specific type of acne and its correlation with progesterone therapy has not been previously reported.

From the Department of Dermatology, Cedars of Lebanon Hospital and Los Angeles County General Hospital.

Read before the Section on Dermatology and Syphilology at the 102nd Annual Session of the American Medical Association, New York, June 2, 1953.

ADULT PREMENSTRUAL ACNE

Under the title "adult premenstrual acne," we have differentiated three main groups. First, the clinical features applicable to all three groups will be described: This form of acne makes its appearance in adult women between the ages of 20 and menopause. Aside from complaints referable to the menstrual cycle the general health of these patients is good. The lesions are confined to the face and may make their appearance at any time during a two-week period preceding the onset of menstruation. However, the eruption characteristically appears within 10 days prior to the onset of the menstrual flow. Approximately 50% of the patients complain of some symptom of menstrual disturbance such as premenstrual tension, dysmenorrhea, menorrhagia, scanty menstrual flow, or irregularity of the interval between the periods. The eruption consists of firm painless erythematous dome-shaped deep discrete papules, papulonodules, or nodules which occasionally become cystic. The most important feature is the development of the lesion without a pre-existing comedo. The lesions require about three to four days for their evolution and range from 4 to 15 mm. (average 7 to 9 mm.) in diameter. Generally only two to three lesions appear prior to one menstrual period; rarely do more than six occur at one time. The individual lesion involutes spontaneously by resorption in about three weeks, but may persist in some instances as long as eight weeks. Healing occurs as a rule with temporary residual erythema or pigmentation, without scarring. The commonest sites involved are the chin, the sides of the face, and between the eyebrows. The eruption is not symmetrical. If an involved area is incised a scanty serosanguinous material can be expressed. Occasionally the cystic type of lesion will contain some purulent sebaceous material.

The patients in this study can be divided into three main groups:

Group 1.—Those in whom the premenstrual papules, nodules, and/or cysts begin for the first time in adult life (after the age of 20). There is no concomitant or previous history of acne vulgaris, i. e., comedone acne.

Group 2.—Those in whom the "premenstrual type" of lesion (described in Group 1) plus the usual comedones of acne vulgaris begin concomitantly in adult life. There is no history of acne during the adolescent period.

Group 3.—Those in whom acne vulgaris began during adolescence and persisted into adulthood, through the early or midtwenties. During this latter period, the "premenstrual type" of lesion made its appearance and persisted, even though the comedo acne disappeared (with or without treatment).

MATERIAL AND METHOD

This report is based on the study of 95 women ranging in age from 20 to 51. Sixty-two of these patients had received full courses of roentgen therapy. In addition, these women had received all or part of the following treatments: hot and cold quartz ultraviolet irradiation, administration of vitamin A, thyroid, estrogens, desquamating lotions, ointments, vaccines, arsenicals, and dietary restrictions. These patients comprised a group which we heretofore classed as treatment-resistant acne because of the cyclic appearance of papular and/or cystic types of lesions despite the above-named modes of therapy.

The treatment used for the control of the entity we are describing has been the administration of progesterone. A dose of 10 mg. of progesterone (10 mg. per cubic centimeter of sesame oil) was injected intragluteally 10 days before the onset of menstruation, and a dose of 5 mg. was repeated five days before the menstrual period. If the injections inhibited the formation of the premenstrual lesions we substituted 10 mg. progesterone buccal tablets daily for 10 days preceding the menses. The tablets were not as consistently effective as the injections, and on occasion it was necessary to return to the intramuscular route.

ANALYSIS AND RESULTS OF TREATMENT

Only 45 of the 95 patients (or approximately 50%) complained of disturbances associated with the menstrual cycle, such as irregularity of the interval between the menses, scanty or excessive menstrual flow, dysmenorrhea, or premenstrual tension and headaches. Frequently, the patients spontaneously commented on their relief of premenstrual tension, headaches, or dysmenorrhea following progesterone therapy.

The number of injections given a person ranged from 1 to 29. The smaller figures usually meant that the control of the acne was satisfactory, and that buccal progesterone tablets were substituted. The greater number of injections were required for the control of the acne in only a few patients, i. e., when the buccal tablets were ineffective. Fifty-five patients received both injections and tablets. Three patients in whom the tablets were ineffective were promptly controlled as soon as intramuscular injections of progesterone were resumed. (The results were consistently better when the drug was injected.) The failure of oral therapy in some patients is probably explained by inadequate dosage due to poor absorption or improper use of the tablets by the patient. There was no correlation between the extent and the duration of the eruption and the results obtained.

Group 1.—There were 36 patients in this group. Except for one, these women ranged in age from 35 to 51. In all instances there was no previous history of acne vulgaris. Aside from an occasional comedo, their lesions consisted of inflammatory firm papules, nodules, and/or cystic lesions, the onset occurring within a 10-day period prior to menstruation. The site of predilection was the chin. The duration of each lesion was approximately one month; so that at the time of involution a new crop of lesions would appear. Involution of some lesions required as long as two months. Twenty of the 36 patients complained of menstrual difficulties. The eruption was completely inhibited by the administration of progesterone during the corpus luteum phase of the menstrual cycle and in 50% of these patients by the buccal tablets alone.

Group 2.—This group included 15 patients. As in the previous category, none gave a history of acne during the adolescent period. However, in these patients there was a mixture of the type of eruption described in Group 1—i. e., noncomedo acne—and the lesions seen in acne vulgaris—that is, comedones, papules, and papulopustules. Their ages ranged from 23 to 35. Except for one, all the patients in this group had roentgen therapy prior to consulting us or were given roentgen therapy by us. It was in this group and in Group 3 that the specificity of progesterone in inhibiting the "premenstrual type" of lesion described was clearly demonstrated. It was particularly apparent because roentgen rays and other conventional treatments were effective in most cases in resolving the (comedo) "acne vulgaris type" of lesion, but had no effect in preventing the monthly appearance of the (noncomedo) "premenstrual type" of lesion.

In only one patient of this group was there a failure of inhibition of the acne lesions with progesterone.

Group 3.—This group consisted of 44 women ranging in age from 20 to 40. In this category acne vulgaris began early in adolescence, disappearing at the end of the teen-age period or persisting in adult life. In one group of patients the pre-

menstrual papular, nodular, and/or cystic lesions appeared as the common comedo acne was waning. In another class, the premenstrual type of lesion made its appearance 1 to 10 years after the teen-age comedo acne had subsided. Here again, it was found that roentgen rays and other acne treatment were ineffective in preventing the cyclic outbreaks of the "premenstrual type" of lesion.

In this group of patients progesterone therapy failed to inhibit acne lesions in two. In one of these patients an exacerbation of the eruption was produced by injections of progesterone.

Side-Effects from Progesterone.—The most frequently encountered side-effect from progesterone was a shortening of the interval between the menses. Seven of the 95 patients observed that their menstrual periods occurred prematurely. In two patients breast pain and menorrhagia occurred repeatedly following administration of progesterone. Gynecological studies of these two patients uncovered the presence of endometriosis. A prolonged interval between the menstrual periods occurred in two patients. Dysmenorrhea was encountered only once. Breast pain was the only untoward effect which necessitated curtailment of hormone therapy. The other side-effects did not necessarily appear with regularity following progesterone administration.

COMMENT

Progesterone was effective in preventing or controlling the condition we have termed "adult premenstrual acne" in the majority of patients. Therapy with progesterone varied from 5 to 20 months. Many patients discontinued therapy of their own accord after noting absence of lesions for two or three months. In most instances, upon relapse of the eruption, therapy was promptly resumed. We are not in a position at the present time to state whether progesterone has provided a clinical cure for this type of acne; the follow-up period is still inadequate. We are more impressed, actually, with the inhibiting influence of progesterone and the theoretical implications in the type of acne we have described. From this group of 95 patients, 12 showed no evidence of relapse after treatment was discontinued. The longest interval of freedom from lesions in any patient after cessation of progesterone therapy was 14 months. In four, relapse was noted approximately one year after hormonal treatment was curtailed.

Among our group of patients, a spontaneous remission of this type of acne occurred in five women during pregnancy, only to recur within several months after term. It should be noted that during pregnancy the progesterone blood level remains at a maximum concentration.

The occurrence of these papules, nodules, and/or cystic lesions within the period before the onset of menstrual flow coincides with the time when the progesterone level in the blood is nearing its maximum concentration. The secretion of the corpus luteum hormone begins at the time of ovulation and ceases at the time the corpus luteum degenerates. This suggests that the corpus luteum and/or its derivatives (progestins) may be at fault. The assumption that a deficiency of the corpus luteum hormone might exist resulted in our use of progesterone in treatment. We have not found progesterone to be effective in controlling the lesions of the usual acne vulgaris, nor has it been effective in patients in whom a definite history of premenstrual exacerbation has not been obtained. We have not found progesterone effective in controlling the commonly occurring premenstrual flare-ups of the usual

comedo type of acne vulgaris. In short, we have found progesterone effective only in the clinical picture we have described under the title "adult premenstrual acne." Progesterone therapy for acne has been reported before, but the equivocal results are probably due to the use of this hormone in comedo acne. Johnson recently reported that he had treated nine cases with progesterone and had obtained good results. It is interesting that he concluded that progesterone probably will be found most useful in the older patient with acne. It is very likely that the group of patients he reported was similar to ours.

Goldzieher found that prolactin controlled premenstrual acne in a special group of patients in whom acne was associated with menorrhagia and dysmenorrhea. He concluded in another report that the effect of prolactin would seem to be based on luteotrophic properties of the hormone which support or correct the function of the lutein body.

An explanation for the favorable effects of progesterone which we have observed is necessarily dependent on our present-day knowledge of the effects of progesterone in general. Its major effects are related to the organs most concerned with gestation. Adequate information concerning its functions in humans is far from complete. In humans, the presence of progesterone is determined either by (1) examination of the endometrium for secretory activity during the luteal phase of the cycle or (2) by measuring pregnanediol, an excretion product of progesterone. Since progesterone is always preceded or accompanied by estrogen it is difficult to determine which of its actions are direct. The favorable effect of progesterone in our patients may not act as a supplemental therapy during the luteal phase at all, but perhaps by an entirely different mechanism.

Perhaps the type of eruption we have described may be related to the retention of salt and water. The salt-and-water-retaining powers of progesterone, estrogens, and other steroids is well known. Way and Andrews state that this retention may be an important causative factor and of significance in acne seen near the time of menstruation. However, we have never encountered this type of acne in the numerous corticotropin (ACTH)- or cortisone-treated patients, wherein the degree of salt-and-water-retention was extremely marked.

We feel that progesterone has an inhibiting effect on the specific type of acne that we have described. It is very possible that a mode of administration of progesterone other than our method may achieve better results. It is possible that other combinations of estrogens and progesterone, such as the administration of estrogen in the first half of the cycle followed by progesterone in the second half or combinations of progesterone and estrogen in the luteal phase of the cycle may have better therapeutic effects. Since prolactin has luteotrophic properties, it also may prove to be beneficial. We feel that studies along these lines are worthy of further investigations.

SUMMARY

A specific type of noncomedo adult premenstrual acne has been segregated from the group of acnes.

This type of cyclic acne occurs in women between the ages of 20 and 50 and consists of papules, nodules, and/or cystic lesions, developing without preexisting comedones.

This entity has been classified into three clinical groups.

Administration of progesterone starting approximately 10 days prior to the onset of menstruation was effective in controlling the eruption in the majority of patients.

436 N. Roxbury Dr.

ABSTRACT OF DISCUSSION

DR. GERALD M. FRUMESS, Denver: Dermatologists agree that the endocrine system plays an important role in most forms of acne vulgaris. We need feel no embarrassment at our uncertainty as to what hormone to use in treating which type of acne. Our confusion is no worse than that of gynecologists, who differ in the approach to functional uterine bleeding due to endometrial hyperplasia—a syndrome supposedly due to the unopposed action on the endometrium of too much estrogen.

One group advocates the use of progesterone, since it converts the excess of circulating estradiol into soluble estrone and estriol, which are then eliminated by the kidneys.

A second school proposes the use of large amounts of estrogen in order to inhibit the activity of the anterior lobe of the pituitary gland and thereby suppress the ovaries, which are the main source of estrogen.

A third faction favors the administration of testosterone in order to produce atrophy of the endometrium and "neutralization" of the ovarian hormone.

And a fourth group uses a combination of all three of these hormones; why, I do not understand.

Thus we may take pride if, indeed, dermatologists have delineated a type of acne vulgaris which responds with even admittedly moderate uniformity to one of these endocrine agents. My colleagues and I reported discouragingly on progesterone therapy of acne vulgaris in 1951. I am not thereby prejudiced against the authors' results. Our cases were not selected on the same basis as were those of Drs. Newman and Feldman; though a review reveals that a number of our patients fell into Group 3 described in the paper under discussion. Second, we administered progesterone at weekly intervals rather than only during the luteinizing phase of the menstrual cycle.

I should like to ask the authors whether their most favorable results were achieved chiefly in women with hyperestronism. These women, through poor liver function, vitamin B deficiency, or general undernutrition, produce too little estrase, which normally destroys estrogen, thereby permitting hyperestronism to develop. Endocrinologists tell us that these women are of the excessively feminine type—in an unglamorous sort of way—subject to asthenia, dysmenorrhea, and acne. In these persons progesterone should be of value because of its ability to convert the excess estradiol into soluble estriol which can then be excreted, and because progesterone suppresses anterior-pituitary activity and thereby prevents further ovulation and hence additional production of estradiol.

We now reach an apparent paradox; for if progesterone is effective in treating adult premenstrual acne with hyperestronism, then the much less costly diethylstilbesterol, given in large doses—to the amount of 10 mg. daily starting at the midinterval—should be equally effective, for such doses suppress ovulation by diminishing the activity of both the anterior-pituitary gland and the ovaries. Small doses of diethylstilbestrol, on the other hand, stimulate these two glands and should, theoretically aggravate this type of acne.

It is to be hoped that the results of Drs. Newman and Feldman will be confirmed by others and that a sequel will be a more thorough understanding of the physiological process involved. Perhaps we shall then establish the safest effective means of restoring endocrine balance in this type of acne, be it by the use of progesterone, large doses of estrogen, still other hormones, or their combinations.

DR. M. B. SULZBERGER, New York: I think that Dr. Frumess' discussion of the very excellent paper by Newman and Feldman brings out very well the tremendous complexity of the situation with regard to the use of these hormones, whether by endocrinologists, gynecologists, dermatologists, or others, and whether it be in the treatment of acne or of other diseases. I fear that what I am going to say is only going to add more complications to this already complex situation.

In the first place, the recent experience of Rothman can be mentioned in this connection. In treating rats—rats, of course, are not human beings—locally with steroid hormones and then studying very carefully the effect of the administration of these steroids upon the sebaceous glands and hair follicles of the animals, Rothman and his associates could show (very convincingly, I believe) that there was a tremendous increase in size of the sebaceous glands under the influence of testosterone locally and under the influence of progesterone locally; whereas there was either no increase or even a diminution of the size of the sebaceous glands under the influence of cortisone and estrogenic steroids.

Of course, it is quite apparent that those agents which stimulate the pilosebeceous apparatus would be those most inclined to produce or aggravate acne of various kinds, so here we have a situation in which progesterone goes parallel with testosterone in its effect on the structures which are concerned in acne.

In consonance with these hypotheses, Aaron Brunetier, of France, has recently reported his observations that acne is made worse by the administration of progesterone.

Formerly, I used to teach that eunuchs, because their testes have been removed, don't get acne; and that is a fact. They have no testosterone, no testicular androgens from the testes, which have been removed.

Now the question is, why do females—who have no testes—still get acne? The answer to that used to seem every simple to me, although I realize now how illogical I was. I thought that the reason the females got acne was because of their adrenocortical androgenic steroids. If I had thought further and more clearly, I would have realized that this could not be the explanation, because, after all, the eunuch has no less adrenocortical steroids than the female or the non-castrated male. So one is obliged to postulate some other influence producing acne in females, who have no testicular androgens. As far as I can see, it is unlikely to be their adrenocortical androgenic steroids.

On the basis of these considerations it was logical to suppose that the female hormone progesterone might be the one most implicated in female acne. That also seemed to be the basis of Rothman's conclusions from his experiments.

I think there is a possibility that all the earlier findings as well as those of Drs. Newman and Feldman may some day be reconciled despite their seeming contradictions.

Perhaps when one injects certain doses of progesterone, one reduces the susceptibility or sensitivity of the pilosebaceous apparatus in its capacity to respond to progesterone or progesterone-like steroids. You know that sometimes one can specifically desensitize with an injection. It may not be simple hormonal replacement that Drs. Newman and Feldman have been carrying out, but a measure which brings about an alteration in the capacity of the affected tissues to respond to the agent which they have injected.

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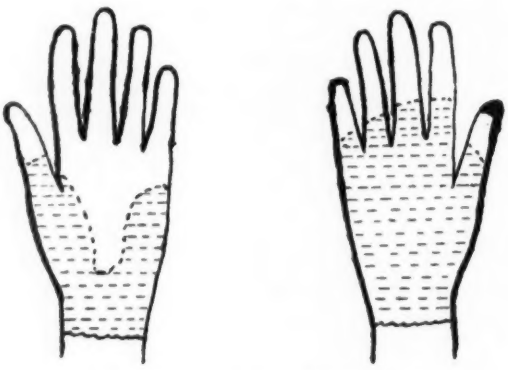
Clinical Notes, New Instruments and Techniques

TRICHOPHYTON RUBRUM INFECTION TREATED WITH REFRIGERATION WITH LIQUID NITROGEN

LOUIS G. JEKEL, M.D.
PHOENIX, ARIZ.

Many types of treatment have been advanced for skin infection with Trichophyton rubrum, the large number of methods being mainly due to the fact that the condition is notoriously resistant to treatment. No reports were found of treatment with refrigeration. Haxthausen [1] did use carbon dioxide snow in the treatment of ringworm of the scalp, the organism being a Trichophyton. He produced a kerion type of reaction and concluded that the beneficial effect was due to stimulation of host tissue resistance. Creeping eruption is an infestation commonly treated with cryotherapy. By and large, however, the method has not been extensively adapted to use in either infections or infestations. Hence this report.



Left hand: front (left) and back (right).

REPORT OF CASE

H. S., a white man 45 years of age, was examined on July 22, 1952. His eruption had begun four years before while he was residing in Indiana. Several weeks before examination his hands had become secondarily infected. His family physician administered penicillin. A few days later he developed an acute, widespread urticaria. He was placed in a hospital and was treated with corticotropin (ACTH) and cortisone. The urticaria subsided; the patient left the hospital, and treatment was discontinued. Soon the urticaria reappeared in a less severe form and the patient was referred to me.

Examination revealed round or oval lesions up to 4 in. (10 cm.) in diameter on the hands and forearms. These lesions were erythematous macules with raised borders. The left hand was extensively involved, as indicated in the accompanying Figure. A diagnosis of mycotic dermatitis was confirmed by culture, the offending organism being T. rubrum.

Routine dermatological treatment, including superficial roentgen therapy, resulted in the disappearance of all lesions except those on the left hand (Figure). After three months of standard treatment had failed to effect a cure of these remaining lesions on the left hand, cryotherapy was instituted in that area with applications of liquid nitrogen. Treatments were administered on Oct. 21, Nov. 5, 12, and 18, Dec. 3, 1952, and Jan. 8 and 23, and Feb. 5, 1953. On the last three dates only small areas of residual infection required treatment.

Itching, which had been severe, disappeared soon after the first application of liquid nitrogen. Three months after the last treatment no evidence of infection remained. There were no scars.

SUMMARY

A patient with a Trichophyton rubrum infection of long standing was treated successfully with application of liquid nitrogen. It is believed that this method may be useful in many such cases when the involved area is of limited extent.

Professional Building.

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INFLAMMATORY RINGWORM DUE TO TRICHOPHYTON FAVIFORME

Report of Three Cases in One Family

WILLIAM SAUNDERS, M.D.
WATERTOWN, N. Y.

In 1952, Muskatblit and Fisher[1] published a well-described case report of two members of a family with infection caused by Trichophyton faviforme. They stated that T. faviforme has rarely been isolated in the United States and that no previous cases had been reported in the New York area.

The present report closely parallels that of Muskatblit and Fisher, who described a 7-year-old child with kerion of the scalp and lesions of the glabrous skin. There was also an erythematous, vesicular eruption of the glabrous skin of the child's mother. The present report includes kerion of the scalp and glabrous lesions of a 5-year-old child; in addition, there were glabrous lesions of the mother and of a baby sister.

REPORT OF CASES

CASE 1.—R. B., a 5-year-old white farm boy, was first seen on Jan. 17, 1952. He was referred by a surgeon who, having hospitalized and incised a very large carbuncle-like lesion of the scalp, then recognized that the scalp eruption was out of his line. The boy had two boggy pustular areas of the scalp: One on the right side, 4 cm. in diameter, was very much raised and contained a deep linear incision; the other boggy lesion measured about 3 cm. and was located on the rear of the scalp. In addition, there were four nonraised, crusted scaling patches of the scalp; two scaling, erythematous patches of the forehead; one small, scaling patch behind and slightly inferior to each ear, and one similar patch of erythema and scaling on the right side of the back.

Preliminary examination of the hair from the kerionic areas showed chains of spores having the appearance of a megasporon, ectothrix infection suggesting Trichophytum gypseum. Inquiries about cattle infection yielded the information that some cattle had crusted lesions. Examination of hair from these areas failed to reveal fungi.

Culture on Sabouraud's medium of hair from the kerionic areas revealed slowly growing, small, glabrous, gray colonies of a rubbery consistency. There was a small central yellowish-gray velvety elevation and a few irregular radial rugae. The border zone showed feathery radiations submerged within the medium. Microscopic examination of a culture mount revealed relatively simple elements: branching hyphae with septations and a moderate number of chlamydospores without fuseaux or microconidia. A laboratory diagnosis of T. faviforme infection was made.

CASE 2.—C. B., aged one year, a sister of the first patient, was first seen on Feb. 11, 1952, complaining of an erythematous, scaling patch measuring 2.5 cm. on the right cheek. There

was also a smaller scaling eruption of the left cheek. These had been noticed about two weeks previously. Direct microscopic examination of scales showed septate hyphae of the ringworm type. Culture did not grow.

CASE 3.—A. B., aged 34, mother of the above two patients, was first seen on Feb. 11, 1952, complaining of an erythematous, vesicular patch measuring 2.5 cm. on the left side of the upper, anterior chest. This had its onset shortly after the eruption began on the baby's cheeks. Direct microscopic examination showed septate hyphae of the ringworm type. Culture did not grow.

TREATMENT

Treatment of the boy with kerion and glabrous lesions was effective in nine weeks, when regrowth of hair was noted. Wet dressings of bichloride of mercury and manual epilation were used on the scalp and alcoholic proprionate-caprylate solution was used on the rest of the areas. The baby developed contact dermatitis from sulfur-salicylic acid ointment and the mother was sensitive to Asterol (2-dimethylamino-6-[β-diethylaminoethoxy]-benzothiazole) dihydrochloride ointment (patch test showed this to be due to the Carbowax base). Both of these patients improved readily with undecylenic acid ointment treatment.

SUMMARY

Three cases of ringworm infection in one family are reported. T. faviforme was cultured from the lesion of a 5-year-old boy who had contact with cattle which had crusted lesions. A one-year-old sister, who had no contact with animals, became infected with a ringworm type of fungus, presumably by direct contact with the original patient. The mother of these children became infected with a ringworm type of fungus, presumably by direct contact with the baby's cheek against her upper chest. Although cultures from both the latter patients failed to grow, it may be reasonably assumed that they, too, were infected by T. faviforme.

These cases are presented to supplement the report of Muskatblit and Fisher [1] inasmuch as T. faviforme has rarely been isolated in the United States, particularly from this section.

535 Woolworth Building.

ADDENDUM

Since this report was submitted, a family of five, including a boy with kerion of the scalp, was found to be infected by T. faviforme.

In addition, in 15 patients with positive cultures for fungi reported in 1953 in Jefferson, St. Lawrence and Lewis counties in northern New York state, 8 had ringworm of the scalp. All positive cultures of the scalp were caused by T. faviforme. In addition, five cultures of the glabrous skin were positive for T. faviforme.

These reports would indicate that, in this section of New York state, T. faviforme infection is not uncommon.

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COMBINED BACITRACIN-NEOMYCIN OINTMENT IN TREATMENT OF PYOGENIC INFECTIONS OF THE SKIN

J. M. GREENHOUSE, M.D.
AND
W. C. RYLE, M.D.
ST. LOUIS

Bacitracin is quite effective locally against a wide variety of Gram-positive micro-organisms, including Staphylococcus, beta hemolytic Streptococcus, Pneumococcus, Clostridium welchii,

Studies, observations and reports from the Barnard Free Skin and Cancer Hospital and the Division of Dermatology, Department of Medicine, Washington University School of Medicine.

some of the actinomycetes, Treponema pallidum, and others. Its nephrotoxic properties and irritative local effects when injected intramuscularly have precluded its use except as a topical application, where it has been used with great success.

Neomycin is very effective locally against Gram-negative and Gram-positive organisms. However, the hepatotoxic and ototoxic properties of neomycin preclude its systemic adminstration. Some patients with hemolytic Streptococcus and B. pyocyaneus (Pseudomonas aeruginosa) infections, in a series treated by Kile, did not respond satisfactorily to neomycin ointment.

Since both bacitracin and neomycin are not used systemically and since the two together are effective against all Gram-negative and Gram-positive organisms, a combination of the two in a petrolatum ointment base containing 500 units of bacitracin and 5 mg. of neomycin sulfate per gram of base * was tried in a series of 53 patients with various types of pyodermas. Out of the 10 patients with impetigo, all were well at the end of 10 days. Of seven patients with infectious eczematoid dermatitis, six cleared within two weeks; one did not improve, and the treatment was changed. Ten patients with secondarily infected atopic eczema were cleared of their secondary infection within one week. The secondary infection superimposed on dermatitis venenata in four patients was cured in five days. Five patients with folliculitis were well at the end of one week, and at the end of two weeks two other patients with folliculitis were not improved. Four patients with ecthyma were well at the end of 30 days. Of the two patients with secondarily infected infected seborrheic dermatitis, one healed in 10 days and the other showed no improvement. One patient with furunculosis, who also received intramuscular penicillin, was cleared in one month, and another patient with multiple furuncles was healed in 11 days. A patient with acne vulgaris, who also received intramuscular penicillin and sulfisoxazole (Gantrisin) by mouth, improved after one month. Another patient with an infected scar on the lower leg was cleared after two weeks. The infection secondary to an ingrown toenail in one patient was cleared within one week. A pyoderma in a diabetic patient was healed in one month. An infected sebaceous cyst was cleared within one week, and a secondarily infected fissure in the perianal area of a patient from a pilonidal cyst was well within two weeks. One patient with secondarily infected neurotic excoriations was cleared within one week. There was no improvement in the radiation necrosis occurring in a year-old radium scar after two weeks.

The results compare favorably with those with other antibiotics used locally and reported to date. Moreover, no cases of sensitization or primary irritation occurred. Since this is a preliminary short series, it is too early to state what sensitization rate will result, but on the basis of sensitization indices of bacitracin and neomycin when used alone a very low sensitivity rate is to be expected.

SUMMARY

A new antibiotic ointment containing both bacitracin and neomycin resulted in a cure rate of 88% when used topically in a series of 53 patients with various types of pyodermas.

Forty-seven patients, four of whom received intramuscular penicillin simultaneously, cleared completely in a time interval varying from two days to two months. Six patients, including one that received penicillin, failed to improve.

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* Bacimycin ointment. Walker Laboratories, Inc., Mt. Vernon, N. Y., supplied the material used in these studies.

SURGICAL AVULSION OF THE NAIL

A Modified Technique

ABNER KURTIN, M.D.
NEW YORK

Surgical avulsion of the nail is a not uncommon therapeutic necessity. The nail is usually removed by traction after it has been bluntly separated from its bed. The infected nail is friable, and often difficult to remove. It crushes easily under the pressure of the hemostat, and adequate traction may be impossible to obtain. Piecemeal removal, then, is necessary, which increases the possibility that infected spicules will be left behind to reinfect the new nail. Profuse bleeding may occur after this procedure.

It is common knowledge that a fingernail will loosen and separate cleanly after injury severe enough to produce a large subungual hematoma. The hematoma acts as a blunt dissector, and, thus efficiently separates the nail from the bed. In an effort to duplicate this natural process, a subungual injection of water was attempted. Enough pressure to separate the nail was difficult to obtain, and fluid escaped backwards along the path of the needle. The cement substance which binds the nail to the bed proved an effective barrier to the penetration of water. A solution of hyaluronidase was then successfully used in an attempt to break this barrier.

PROCEDURE

The digital nerves are blocked in the usual fashion with 2% procaine solution. The hyaluronidase (100 turbidity units per cubic centimeter of distilled water) is then injected under the distal end of the nail. The injection should be given after the needle (25 gauge) has penetrated ¼ in. (0.64 cm.). The needle should be in contact with the inner surface of the nail at all times. The fluid spreads quickly and soon escapes from the eponychial folds. During the injection, the needle should be advanced slowly until the injection of 1 cc. of the liquid is completed. After a few minutes, the nail can be cleanly removed by gentle traction. Bleeding is minimal.

945 Fifth Ave. (21)

RECKLINGHAUSEN'S DISEASE IN THE NEGRO

DARIO ARGÜELLES-CASALS, M.D.
HABANA, CUBA

Recklinghausen's disease is classified as a rare disease in the Negro. American dermatologists with wide experience among Negro patients report seeing this condition infrequently. Lewis [1] surveyed the literature in 1942 and found that only three cases had been reported among the Negro race: Weiss,* in 1921, reported two typical and extensive cases in Negroes—one of a woman, aged 22, and the other of a man, aged 46. Another case in a Negro has been described by Heuer and Bell.† Niedelman [2] added a fourth Negro case. A search of the literature has failed to reveal any additional reports of Recklinghausen's disease among Negroes.

I have seen five Cuban Negroes with Recklinghausen's disease, and herein report these cases.

REPORT OF CASES

CASE 1.—C. F., a 32-year-old Negro woman, stated that as far back as she could remember her body had been covered with numerous "lumps."

A physical examination revealed multiple areas of black pigmentations, ranging in diameter from that of a pinhead to that of a half-dollar, associated with molluscum fibrosum scattered

* Weiss, cited by Lewis.[1]

† Heuer and Bell, cited by Lewis.[1]

on the arms, trunk, and legs. The tumors varied in size from a pinhead to a hen's egg. Some of the growths were small nodules in the subcutaneous tissue. Two were soft and gave the impression of being mammillated. The patient stated that her parents, three sisters, and two brothers were not similarly affected. The patient is mentally retarded and has a twin sister who has epilepsy.

CASE 2.—J. M., a Negro man aged 37, has had Recklinghausen's disease since birth. Multiple hyperpigmented spots and molluscum fibrosum were scattered on the trunk and extremities. The other findings were cutis verticis gyrata and positive serologic reactions for syphilis.

CASE 3.—C. G., a Negro man aged 21, had small neurofibromas (Recklinghausen's) and pigmented spots of assorted sizes on the body. There was also hyperlaxity of joints. The mother and maternal great-grandmother were said to have had similar skin lesions, suggesting Recklinghausen's neurofibromatosis.

CASE 4.—A. O., a 17-year-old Negro girl, presented hyperpigmented spots and neurofibromas, varying in size from that of a pinhead to that of a large pea, on the trunk, face, extremities, and palms. The intelligence of the patient was of low average, the palate showed a high narrow vault; she had hyperhidrosis of the palms. Two brothers were found to have retinitis pigmentosa; her mother, who died many years ago, had hemophilia.

CASE 5.—X. Y., a 50-year-old Negro woman, had had Recklinghausen's disease ever since she could remember. The eruption consisted of hundreds of soft, fleshy, and elevated tumors scattered over the face, neck, trunk, and extremities. They varied from the size of a pinhead to that of a dime. There were a great number of black spots 2 to 3 mm. in diameter, distributed on the trunk, face, and extremities.

SUMMARY AND CONCLUSION

The cases of five Negroes with Recklinghausen's disease are reported. This condition is somewhat less frequent in the Negro than in the white race, but it is not nearly so uncommon as had been stated.

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CSILLAG'S DISEASE

Report of a Case

MAJOR SANFORD M. VAUGHN

AND

LIEUTENANT COLONEL WILLIAM N. PIPER

MEDICAL CORPS, UNITED STATES ARMY

Wise and Shelmire,[1] in 1928, reported on two cases of dermatitis lichenoides chronica atrophicans (Csillag's disease). They described the condition as being characterized by the formation of a varying number of white, shiny, indurated, round and oval, well-defined papules, appearing in closely agminated groups of individual lesions. The papules are in juxtaposition but do not coalesce; that is, they do not blend together to form large patches. The papules have no areolae; or there may be a faint, pink, peripheral zone, or, more frequently, a zone of hyperpigmentation. Scaling and Wickham's striae are absent; the buccal mucosa and the skin of the genitalia are not attacked. Some of the papules have shallow depressions, but the true dell

Senior Resident of Dermatology and Syphilology Section (Major Vaughn); Chief, Dermatology and Syphilology Service (Lieutenant Colonel Piper), Walter Reed Army Hospital.

formation seen in lichen planus is absent. The lesions do not itch. Punctate depressions, horny plugs, and crosshatching do not play a part in their evolution.

After the full development of the papules, a flattening and superficial shrinkage takes place, so that the outlines of the papules become less distinct, but are not obliterated; the close approximation of several dozen or several hundred flattened papules results in the formation of a smooth, glossy patch of round, oval, or irregular outline and of varying extent. The periphery of such a patch is usually hyperpigmented. A faint degree of resistance is imparted to the finger when these plaques are palpated. In the patches of longest standing and greater extent the surface is smooth, more or less wrinkled, and the skin is soft and dead-white. Some of these individual patches finally coalesce to form large areas of atrophic skin.

The different stages of evolution may be present in the same eruption at the same time; fully developed papules with a well-defined periphery, crops of agminated flattened lesions forming circumscribed patches, and areas of skin undergoing pronounced atrophy, with wrinkling of the surface.

In discussing the relationship of dermatitis lichenoides chronica atrophicans to other conditions which have been variously called "white-spot" diseases, the following were considered:

1. Lichen sclerosus et atrophicus (Hallopeau and Darier)
2. Lichen morphoeicus (Stowers)
3. Lichen planus atrophicus
4. Lichen albus (Zumbusch)
5. White-spot diseases (Johnston and Sherwill)
6. Cardboard scleroderma (Unna)
7. Scleroderma guttatum
8. Lichenoid scleroderma associated with early atrophy

Wise and Shelmire think these dermatoses permit a clinical classification, on the basis of their gross cutaneous manifestations, under three heads: (1) those which show kinship to scleroderma or morphea; (2) those which show kinship to lichen planus, and (3) those which show kinship to neither scleroderma in the literal sense of the word, implying "hard skin," nor to any form of lichen planus. The last group, instead of representing a transmutation of one type of disease to the other, is in reality a distinct clinical entity. The authors conclude that, while dermatitis lichenoides chronica atrophicans is probably an aberrant form of scleroderma, it shows certain features that clinically are not characteristic of scleroderma and pathologically show involvement of both collagen and elastic tissue, as compared with scleroderma, in which collagenous tissue is primarily involved and the elastic tissue is relatively unharmed.

MacKee and Wise [2] reviewed the subject of "white-spot disease" and concluded that all recorded cases could be divided into two groups: (1) the lichen planus group, and (2) the scleroderma group. In a later report, Wise and Rosen [3] felt that differentially these conditions should be grouped as "(1) primary lichen sclerosus, possessing flat, white glistening spots, some of them slightly elevated, and resembling circumscribed scleroderma; (2) secondary lichen sclerosus, possessing the elementary lesions of lichen planus of the Wilson type; (3) the cardlike scleroderma of Unna, or morphea guttata, and (4) the lichenoid form of scleroderma guttata."

Ormsby, in discussing the two cases reported by Wise and Shelmire, stated that in one case shown there was no question of the condition being lichen sclerosus et atrophicus or morphea guttata, and agreed with Wise that it should be considered a separate entity. However, in another review of "white-spot disease," [4] he states that there are three distinct diseases characterized by peculiar white lesions: (1) localized scleroderma (morphea guttata); (2) lichen planus sclerosus et atrophicus, and (3) lichen planus with atrophy.

REPORT OF CASE

A 26-year-old soldier, was first seen in the outpatient clinic of Walter Reed Army Hospital two years before because of a dystrophy of the fingernails, characterized by complete and incomplete shedding of the nails, with secondary onychomycosis. This was followed by similar involve-

Fig. 1.—Atrophic lesion of leg in Csillag's disease.

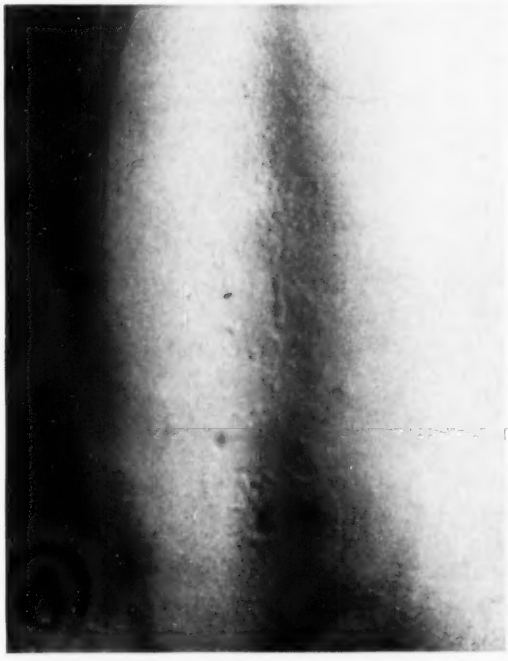

Fig. 2.—Lesions of midlumbar area, posterior, Csillag's disease.

Fig. 3.—Low-power view of leg lesion.

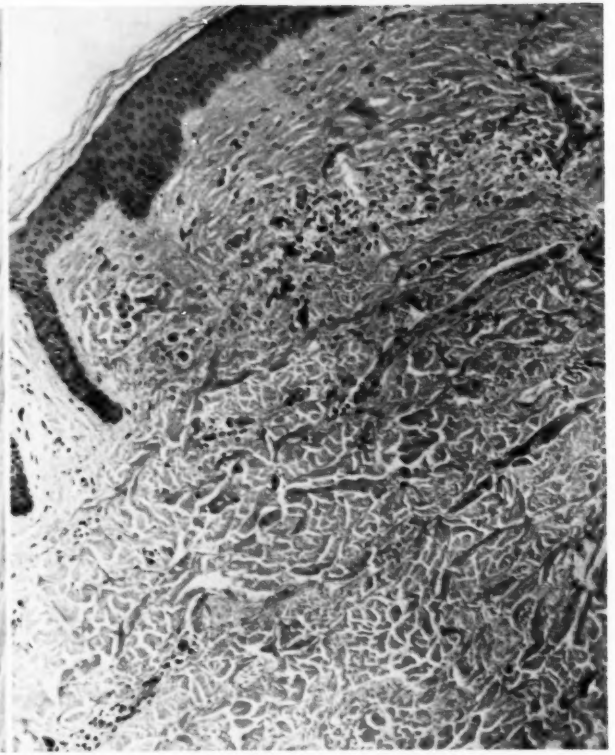

Fig. 4.—Low-power view of a lumbar area lesion.

ment of the toenails a year later, and at that time the patient first noted that the skin over the right shin was becoming thin and easily denuded from slight trauma. During the next few months, his wife noticed that small discrete "white spots" had appeared over the sacral area, and since then there had been a spread over the midline of the lower thoracic area, as well as the upper trunk, posteriorly. The patient was referred for evaluation of the skin condition because of the bizarre appearance.

Physical Examination.—Examination revealed the following: (1) a large, irregular, circumscribed, erythematous to white, glazed and atrophic-appearing plaque involving the middle of the right shin, anteriorly, with small erythematous patches seen in adjacent areas and on the anterior surface of the left leg; (2) small, circumscribed, whitish, atrophic papules and nodules, some showing central delling, some showing coalescence, a few having a linear arrangement, and others showing depression and atrophy with wrinkling of the surface over the midlumbar area, posteriorly, and other small, superficial glazed areas seen scattered discretely over the neck, face, shoulders, and arms; (3) dystrophy of all the nails, some showing separation of the distal edge, some showing lateral fragments, and some being completely absent. Other findings included a mild palmar hyperkeratosis, right, and a harsh, systolic murmur over the aortic area.

Laboratory Data.—Laboratory examination including serological test for syphilis, urinalysis, complete blood cell count, determinations of sedimentation rate, hematocrit, uroporphyrins, blood lipids and cholesterol, total proteins, albumin and globulin, glucose tolerance test, and basal metabolic rate determinations were negative or within normal limits. Trichophyton rubrum was isolated by culture from skin scrapings taken from the feet. Medical consultation was obtained, and no evidence of metabolic disorder was found. The cardiac condition was diagnosed as a possible congenital subaortic stenosis or rheumatic heart disease with aortic stenosis associated with mild left ventricular hypertrophy.

Pathological Examination.—Sections taken from both the large, circumscribed patch on the right leg and an elevated papule on the back were examined with routine hematoxylin and eosin and elastic tissue stains. Both sections were considered to be characteristic of scleroderma. Examination of the section taken from the back revealed the epithelium to be thin and atrophic, with yellow-brown pigment in the lower epithelial layers and loss of rete pegs. The upper corium consisted of loosely arranged collagenous fibers with perivascular round cell infiltrates. Some of the adnexal appendages were atrophic, while the bundles of collagen appeared hypertrophic and sclerotic. There was slight thickening of some of the vessels. Similar changes were seen in the section taken from the leg, except that the adnexal appendages were less prominent and the collagen bundles appeared more hypertrophic and sclerotic. The vessels of the upper corium had a slight infiltrate around them. There was no evidence of elastic tissue change in either of the two sections.

COMMENT

The case of Csillag's disease is reported because it stressed the various clinical aspects associated with "white-spot" disease. The area on the anterior surface of the leg was clinically recognized as circumscribed scleroderma; however, the lesions on the back were clinically recognized only with difficulty. Consequently, disregarding the question of dermatitis lichenoides chronica atrophicans being a distinct entity, the condition certainly seems to warrant a clinical distinction from guttata morphea and lichen sclerosus et atrophicus. No cause for the onychomadesis has been determined.

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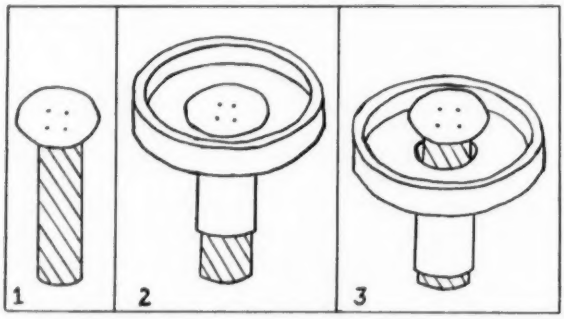
SIMPLE DISTANCE-MEASURING AND CENTERING DEVICE FOR X-RAY THERAPY MACHINE

WILLIAM SNYDER, M.D.
PATERSON, N. J.

I wish to describe an extremely simple method for accurately spacing and centering the tube head of the Profexray skin therapy machine. Although the apparatus which I have devised is not available commercially, it is easily constructed at a cost of less than $1. The device is used with the detachable narrow treatment cone of 15 cm. focus-skin distance, supplied with the machine, and enables one to treat an open field at any chosen longer distance. For illustration, I shall choose a focus-skin distance of 20 cm.

The device consists of a cylindrical block of wood measuring 5 cm. longer than the cone and of such diameter that it just fits inside the cone. A circular piece of tin is nailed to its upper end, serving as a flange to prevent the cylinder from dropping through the cone (Figure *1*).



1, cylindrical block of wood with circular piece of tin nailed to upper end; *2,* cylinder inside treatment cone, ready for attachment to tube head; *3,* manner in which cone is lowered for detachment from tube head of machine.

In operation, the wooden block is placed in the cone, and the latter is attached to the tube head (Figure *2*). The tube head is positioned over the center of the field to be treated, with the lower end of the wooden cylinder touching the skin. The tube head is locked in position; the cone with its cylinder is removed, and the treatment is given. A slight downward movement of the cone is necessary for its detachment from the tube head. Since the cone can slide down over the cylinder, its detachment is accomplished easily without disturbing the position of the tube head or the patient (Figure *3*).

Longer wooden cylinders can be made to provide for 25 or 30 cm. focus-skin distances. If desired, the lower portion of the cylinder may be tapered or be made of clear plastic for better visualization of the center of the field. The device is particularly useful for centering the tube head opening perpendicularly over the Kienböck-Adamson points for x-ray epilations.

555 Broadway (4).

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Samuel J. Zakon, M.D., ***President***

Irene Neuhauser, M.D., ***Secretary***

April 15, 1953

Pityriasis Rubra Pilaris. Presented by DR. MICHAEL H. EBERT and DR. ZACHARY FELSHER.

C. L., aged 10 years, has had an eruption of the face, ears, eyebrows, and upper arms since about the age of 6 months, consisting of tiny hyperkeratotic papules. The onset was gradual, the number of lesions increasing over a period of a few years. There is an associated erythema, but the mother does not remember whether this was present at the start.

The patient's brother, aged 9 months, has a few similar papules but no associated erythema. The father is said to have had "bumps" on the upper arms.

Clinical examination has revealed numerous, closely grouped, tiny follicular hyperkeratotic papules, with an erythematous base, on the face, neck, eyebrows, and upper arms. The degree of erythema varies from time to time. Marked dermographia is present.

At the age of 2 years the patient developed a marked left-sided hydronephrosis because of an external constricting band obstructing the ureter. This was relieved by operation. A congenital cyst of the external urinary meatus was present at birth.

In 1946 the patient was placed on vitamin A therapy, 25,000 units, three times a day and thyroid, ½ grain (30 mg.), daily. This was continued with rest periods over a period of several years. No improvement was noted.

Biopsy revealed a moderately diffuse hyperkeratosis and a follicular plug in a hair follicle. The rete cells showed some vacuolation, and there was edema at the epidermodermal junction. A mild perivascular infiltrate was present in the dermis.

Keratosis Follicularis. Presented by DR. THEODORE CORNBLEET and DR. SIDNEY BARSKY and (by invitation) DR. J. F. SICKLEY.

The patient, V. F., a 32-year-old white man, was admitted to the Cook County Hospital complaining of abdominal pain of one year's duration, hematemesis of six weeks' duration, and melena of one week's duration. He had been troubled with a gastric ulcer since 1943, and in 1950 a gastrectomy was performed. The present symptoms are believed due to a marginal ulcer.

The patient states that since the age of 3 years he has had a skin eruption. It seems to get worse and to improve spontaneously, and the patient believes that each time there is an exacerbation of the skin lesions he has a recurrence of the abdominal pain.

There is little or no subjective discomfort associated with the skin eruption. There is no family history of a similar skin disease.

The patient has received vitamin A therapy in the past and states that there was definite improvement of the skin condition while taking the "tablets."

At present the patient has multiple, slightly pigmented, small (1 to 2 mm. diameter) verrucous lesions that show a tendency to grouping about the shoulders, anterior abdomen, and scapular regions. The face and scalp also show considerable involvement. The extremities are comparatively free of involvement.

There are no dystrophic nail changes bilaterally. Leucoplakial areas are seen on the buccal mucosa. Slight, patchy hyperkeratosis of the palms has been noted.

The urine examination was negative. Blood examination showed 55% hemoglobin, 3,340,000 red blood cells, and 7,950 white blood cells. Kahn reaction was negative. Vitamin A determination was 21; carotene, 133. X-ray of the chest was negative. Biopsy showed keratosis follicularis.

DISCUSSION OF TWO PRECEDING CASES

DR. M. J. REUTER, Milwaukee: The first case was presented as pityriasis rubra pilaris. The individual lesions are certainly suggestive of that diagnosis, but the absence of lesions elsewhere and the fact that this child began to have symptoms at the age of 6 months make me wonder if this is not ulerythema ophryogenes, which I like to think of as a congenital defect of the skin, possibly a form of keratosis pilaris. The only feature that is missing is that there is no atrophy, but that could come in time. These cases are rare. Usually after puberty the disease becomes much less pronounced.

The case of the other patient with Darier's disease was typical. There is one clinical feature of Darier's disease which I do not believe has been emphasized enough and that is that these patients have a photosensitivity. The majority of patients with this disease flare up in the summer time, but they get along very well in winter. Another feature is the presence of these keratotic papules on the palms. I do not believe I have ever seen a proved case of Darier's disease that did not have these discrete keratotic lesions on the palms. These lesions persist indefinitely.

DR. M. H. KULWIN, Champaign: I should like to question the diagnosis, without offering an alternate one, in the first case. One point was the failure of response to vitamin A. Three years ago we had occasion to review (ARCH. DERMAT. AND SYPH. **61**:925-930 [June] 1950) 50 cases of pityriasis rubra pilaris. We found there was a great difference in the time of onset: one major group had the onset before the age of 10 years; the second group had the onset after the age of 40. In the former group the therapeutic response to vitamin A was almost uniformly good, while in the latter group there was no response.

DR. STEPHEN ROTHMAN: It is entirely novel to find hypersensitivity to ultraviolet radiation in Darier's disease. Is not the exacerbation in summer due to heat? Could the ultraviolet sensitivity be demonstrated experimentally?

DR. ADOLPH ROSTENBERG: Are there nail changes with Darier's disease, or is this a manifestation of another dermatosis?

DR. ZACHARY FELSHER: Both Dr. Ebert and I considered our case to be pityriasis rubra pilaris, but we did not know whether to put a question mark after this diagnosis or not. I think the histologic findings point more toward a diagnosis of pityriasis rubra pilaris. There is also some edema at the epidermal junction and some liquefaction of the basal layer which is not usually seen in lichen planus. As far as ulerythema ophryogenes is concerned, this girl is 10 years old. In a period of 10 years there should be some scarring or some alopecia. We wanted to do a dark-adaptation test, but the Eye Department said someone had run off with the apparatus, so we could not get it done.

I am mixed up about the classification of Dr. Kulwin into younger and older groups with pityriasis rubra pilaris. I read over the literature and it seemed to me that Dr. O'Leary said that children with pityriasis rubra pilaris had a congenital disease and that they did not show any vitamin A deficiency in the plasma and did not respond to vitamin A, while older people who got pityriasis rubra pilaris did. However, I do not know whether that classification is exactly correct. I went through several case reports of other dermatological societies, and there were many instances in which vitamin A had not been successful in either younger or older patients.

DR. THEODORE CORNBLEET: Drs. Ebert and Felsher's patient has an odd kind of lesion which I have never seen before in pityriasis rubra pilaris. I do not mean to imply on that account that the condition is incompatible with the diagnosis.

My patient has exacerbations in early spring and late summer. Heat can make Darier's disease worse, but that would not seem to account for his peak periods. I am treating a youth with Devergie's disease who responds capriciously to vitamin A. It did seem to me in his case that thyroid coupled with vitamin A might be of added value. Certainly, the way these patients do on vitamin A does not depend on the blood vitamin A levels. Furthermore, I can say now in these two cases—one of Darier's disease and the other of Devergie's disease—that the liver stores of vitamin A are normal.

Discoid Lupus Erythematosus. Presented by DR. JAMES R. WEBSTER and DR. STANLEY HUFF and (by invitation) DR. STEFAN BIELINSKI.

The patient, A. P., a Negro woman aged 68 years, states that she has had occasional "splotches" on the face for the past two years. About two months ago she developed a red, raised patch on the left cheek which persisted. Shortly afterward she developed similar lesions on both cheeks and about the eyes. The eruption has continued to spread until the present time.

The patient has had diabetes since 1946. It is easily controlled with diet and insulin.

There is a slightly scaling, erythematous eruption of the glabellar, periorbital, and malar areas. The eruption consists of coalesced and discrete patches. The borders are sharply defined, raised, and palpable. Telangiectasia is present in some of the lesions. No atrophy is evident. One lesion on the right cheek has a circinate configuration.

The urinalysis was negative for sugar and albumin. Blood examination showed 82% hemoglobin, 6,500 white blood cells. Mantoux test (1:1,000) was negative. Kahn reaction was negative. Skin biopsy showed lupus erythematosus.

Case for Diagnosis (Lipomelanotic Reticulosis?). Presented by DR. EDWARD A. OLIVER and (by invitation) DR. VICTOR WILLIAMS.

Mrs. R. G., aged 52 years, has the greater portion of her body deeply pigmented, which pigment seems to be melanin clinically and histologically. The pigmentation is diffuse and even, except a few somewhat reticulated areas. There is no infiltration or palpable change, except on wrists where flat papular lesions are superimposed on the pigmentation. The only subjective symptoms are periodic moderate pruritus, especially around wrist. She feels physically fit and well.

The condition began four years ago on thighs and progressed gradually to the present extensive hyperpigmentation of about eight-tenths of the body surface. There is no history of exposure to tar or oils. Since the appearance of hyperpigmentation the patient has been receiving hydralazine (Apresoline) hydrochloride, 50 mg. q.i.d., and conjugated estrogenic substances (Premarin), 1.25 mg., for hypertension and climacteric symptoms, also diphenhydramine (Benadryl) hydrochloride, 50 mg. at times.

Blood examination showed hemoglobin, 70.8%; white cells, 7,250, with a differential count of 58% neutrophiles, 35% lymphocytes, 5% eosinophiles, 2% monocytes; red cells, 3,740,000, with slight hypochromia.

Examination of a histologic section prepared from a biopsy specimen taken from the wrist revealed a slightly thickened scale, a moderate degree of acanthosis, and a very heavy melanin pigment along the basal layer of most of the rete pegs. The superficial blood vessels were dilated and were surrounded by a fairly dense infiltrate consisting mostly of lymphocytes. Perls' test with Prussian blue stain showed the pigment to be melanin.

DISCUSSION

DR. S. W. BECKER: Dr. Oliver's patient is dark-complexioned and has brown eyes. She said when she went out in the sun she tanned quite readily. I believe the pigmentation is chiefly due to the fact that she has a dark complexion. As far as the eruption is concerned, there are a great many possibilities. She said it started on the thigh as a round plaque which did not itch. She said most of the lesions did not itch, though some on the arms and in the axillae did itch.

I do not think it was a drug eruption, certainly not a fixed urticarial type, because she had no itching. She has a very definite erythema over a rather large portion of the trunk. This could develop into some form of lymphoblastoma. There is a very definite lichenoid eruption on the hands and on the forearms. I do not believe there was a microscopic section of this lesion. The other section showed an epidermal melanosis, with round-cell hyperplasia, which might be a forerunner of lymphoblastoma.

DR. KURT WIENER, Milwaukee (by invitation): A year ago some cases of identical pigmentation were described in the *Journal of the American Medical Association*. The authors blamed the chloasma on the antiepileptic drugs. I am more inclined to relate such chloasmas in epileptics with the epilepsy rather than with the medication.

DR. STEPHEN ROTHMAN: In Dr. Oliver's case there is a meshwork of pigmentation, as is seen in livedo reticularis after subsidence of inflammatory processes. A few single lesions of the eruption have a lichenoid character, and I believe lichen planus should be ruled out by biopsy.

In our case I find the diagnosis of chloasma most unsatisfactory. There is a pronounced vasolability in the pigmented areas, and by definition this is not a manifestation of chloasma.

DR. MARCUS R. CARO: I do not believe Dr. Oliver's patient has lupus erythematosus, and the case is not an atrophic lichen planus. Like Dr. Becker, I believe this case will eventuate as a lymphoblastoma. It would be well to obtain a complete blood work-up and to repeat that examination at intervals of a few weeks.

DR. HERBERT RATTNER: Might this not be a case of lipomelanotic reticulosis which often is a forerunner of lymphoblastoma?

If I recall correctly, the cases of hyperpigmentation that Dr. Haxthausen reported some years ago all occurred in patients with encephalitis rather than epilepsy.

DR. THEODORE CORNBLEET: I would like to suggest the diagnosis of acanthosis nigricans. Changes in the axillae and on the breasts are in keeping with it, and the patient looked something less than in good health.

DR. ADOLPH ROSTENBERG: I do not think Dr. Rattner used the term lipomelanotic reticulosis correctly. It is not a skin disease. Without a lymph node biopsy, I do not believe one could make a diagnosis of lipomelanotic reticulosis.

DR. HERBERT RATTNER: I agree that lipomelanotic reticulosis affects lymph nodes, but the first manifestation may be hyperpigmentation of the skin.

DR. ALLAN L. LORINCZ (by invitation): I am willing to agree that this is not Riehl's melanosis. I did not have much conviction about that diagnosis. I think, however, that this is different from ordinary chloasma because of the striking vasomotor disturbance. One might speculate that the melanosis in this case could be post-inflammatory in type with increased local temperature playing a role in stimulating melanin-forming reactions.

Myxedema with Unusual Trichophyton Rubrum Infection. Presented (by invitation) by DR. GEORGE C. WELLS and DR. OLEV R. AAVIK.

D. L., a man aged 51 years, was presented with his twin brother. He was hit on the head by a falling brick 37 years ago, suffered a skull fracture, and was unconscious for several days. Within a year of this accident he began to have convulsive seizures. Since 1930 he has been taking barbiturate medication, with fairly good control of the attacks.

In 1948 he was found to be anemic and was treated unsuccessfully with iron pills and liver-extract injections. Since that time it also was noted that his face, hands, and feet became progressively more puffy and that he was slowing down mentally and physically. His speech slowed, and his voice became husky. Also, since 1948 scaling has appeared and has slowly progressed on his feet, on the right knee, and on two patches on the left thigh.

The patient was hospitalized five weeks ago. On physical examination the blood pressure was 95/65. He has generally coarse, dry, and scaly skin. The face, hands, and feet are somewhat puffy. The tongue is large. The patient appears to be lethargic, but he is well oriented and very cooperative.

His feet show a great deal of dry scaling, both on the plantar and dorsal aspects. This appearance is even more accentuated on the right knee where thick individual scales measure 0.5 to 1.5 cm. in diameter. Two additional patches covered with similar scales are found on the left thigh. There is distortion and discoloration of the toenails and of several fingernails on the left hand.

Laboratory findings were as follows: hemoglobin, 9.1 gm. per 100 cc.; red blood cells, 2,610,000; white blood cells, 4,150, with a normal differential count; Kahn reaction, negative; urinalysis, normal; total protein level, 8.0 gm. (albumin, 4.1 gm. globulin, 3.9 gm.); serum cholesterol, 340 mg. esters, 280 mg.; liver-function tests, normal. The protein-bound iodine was reported too low to read. Basal metabolic rate was —27% on two occasions. Bone marrow normal; spinal fluid, normal; electrocardiogram demonstrated borderline myocardial abnormality, compatible with myxedema.

Examination of scales from the feet and the right knee was positive for fungus filaments. Cultures on Sabouraud's medium showed growth of Trichophyton rubrum. However, the growth of the colonies has been unusually slow. Further mycologic studies on this organism are in progress.

Biopsy of tissue from the lesion on the left thigh showed marked hyperkeratosis, and in the keratin layer there were areas of crust and cell accumulation. The periodic acid-Schiff stain showed mycelium in the horny layer. With the use of toluidine blue there was definite metachromasia of the edematous connective tissue where it appears sparse, with some increase of histiocytes and a few mast cells.

Coccidiomycosis. Presented by DR. SAMUEL BLUEFARB and DR. AARON GOLDBERG and (by invitation) DR. J. F. SICKLEY.

DISCUSSION OF TWO PRECEDING CASES

DR. STEPHEN ROTHMAN: It will be interesting to have a glucose tolerance test done in Dr. Wells's case. In the majority of cases with recalcitrant Trichophyton rubrum (purpureum) infections, we have found a markedly flat glucose tolerance curve (*A. M. A. Arch. Dermat. & Syph.* **67**:239-246 [March] 1953).

DR. DAVID COHEN: We have been interested in this tye of Trichophyton infection. The palms and soles seem much more resistant to treatment than do other parts of the body. In many of our cases one palm is involved, simulating a neurodermatitis or psoriasis. We have been able to culture T. rubrum (purpureum). Clinically these cases are nearly always dry—no findings of vesicles or pustules. There are no subjective symptoms. The patients do not complain of any pruritus either.

DR. M. J. REUTER, Milwaukee: Regarding myxedema, I do not mean to discredit the diagnosis in this case, but it is most unusual to have marked cutaneous symptoms of myxedema with a basal metabolic rate of *— 27*; this rate is usually around — 40.

DR. IRENE NEUHAUSER: The appearance of this patient's palms is characteristic of a Trichophyton rubrum infection. We frequently see industrial patients with this type of palmar infection, allegedly due to contact with some irritant with which the person works. The diagnosis is easily made when the fingernails are involved, but organisms on the palmar surfaces are sometimes difficult to demonstrate. Almost without exception, these patients have thickened scaling patches on the web between the thumb and index fingers. The organism can easily be found in this area.

DR. H. H. RODIN, South Bend, Ind.: I think the most important finding was the elevated cholesterol which is very significant of myxedema.

DR. STEPHEN ROTHMAN: Short-lasting hematogenous showers seem to be a quite frequent event in coccidiomycosis. Such showers, for instance, may cause erythema nodosum. They do not necessarily lead to progressive dissemination with fatal outcome. In one case of mine after the localized pneumonic disease had subsided, a non-painful, noninflammatory pustule appeared on the side of the left index finger. We were able to recover the organism from this lesion. Subsequently there was no further clinical manifestation. The patient has been perfectly well for the last nine years.

DR. GEORGE C. WELLS (by invitation): This man with the myxedema has typical trichophyton lesions of the nails and extremities. We thought that the scaly lesion on the right knee and on the left thigh were atypical, with this unusual amount of dry scaling. We wondered whether the myxedema contributed to the peculiar appearance of the area infected with T. rubrum. We were satisfied that this man had myxedema. His picture has changed since thyroid medication was started. The skin specimen at the time of biopsy showed metachromatic connective tissue mucin. We had many sections; mycelium was found in all of them, stained by means of the periodic acid-Schiff technique and visible in the thickened keratin.

DR. AARON L. GOLDBERG: This young man was presented because of several interesting features: (1) He was employed in the San Joaquin Valley, which is an endemic area; (2) he developed the acute pneumonic form which usually subsides leaving the patient perfectly well (incidentally he received therapy in California which was of the same type as we gave here);

(3) he developed pains and swelling in the joints; (4) he was unfortunate enough to develop systemic manifestations which may involve the lung, central nervous system and skin, such as a subcutaneous granuloma on the chest and in the right inguinal area.

Periarteritis Nodosa. Presented by DR. JAMES K. TOMPKINS (by invitation).

D. T., a white male printer, aged 35 years, noted onset of itching and swelling of hands, feet, and knees four months ago. Associated with this, he noted numbness and tingling of hands and fingers when subjected to cold, heat, or massage, with blanching of the fingers. With the blanching he had noted marked temperature difference in the fingers.

The itching and swelling of the feet subsided about six weeks ago. Three weeks ago he noted the appearance of "bumps" on forehead and scalp.

There is no history of drug intake.

On the forehead there are dilated, tortuous, nodular, pulsating vessels, and on the right side of the occiput there is a pulsating, nodular vessel. The hands are moderately edematous. On massaging, there is blanching of the right index finger, lasting up to three minutes, and marked temperature difference in all fingers, the right index finger being coldest.

Blood examination showed hemoglobin, 12.2 gm. per 100 cc.; red cells, 3,960,000; white blood cells, 5,900, with a differential count of 59% polymorphonuclears, 21% lymphocytes, 2% monocytes, and 18% eosinophiles. Urinalysis showed 1 to 3 red blood cells per high-power field; otherwise the examination was negative. The chest microfilm was negative.

DISCUSSION

DR. FREDERIC T. BECKER, Duluth, Minn.: I do not make a diagnosis of periarteritis nodosa unless I have excluded everything else and have positive histologic evidence to confirm the diagnosis. The usual cutaneous lesions are either nodular, purpuric, gangrenous, or combinations of these. All these findings are variable, and we have recently seen a patient whose presenting evidence was that of a recurrent urticaria at each febrile episode. The other clinical findings vary from hypertension, blood cells in the urine, intermittent fever, and in about 20% of the cases an eosinophilia over 10%. The diagnosis can be established only by histologic findings which show a thrombotic process in the cutaneous vessels, with degenerative changes in the muscular coat. The picture is that of a focal vasculitis, with necrosis of the media and intima. The patient presented today has intermittent pains and swelling in his hands and feet, which seem to be worse on exposure to cold and which appear to be like a physical urticaria of the angioneurotic type. There is a marked prominence of the temporal artery, such as is seen in temporal arteritis; however, there is pain on palpation and tenderness over the area, and this condition usually occurs in a much older age group. Clinical findings add up to a possible periarteritis nodosa or else a temporal arteritis, with angioneurotic edema or some other peripheral vascular disturbance. I believe that biopsy of a temporal artery specimen is indicative to make a proper diagnosis.

DR. STEPHEN ROTHMAN: We have shown this patient before all examinations have been completed, because the Society will not meet for several months, and we thought that the case is most instructive as an example of early incipient periarteritis nodosa. Functional vasoneurosis can be ruled out with certainty. The fingers blanch on pressure, and the blanching persists for several minutes; hence, there must be a fault with the artery. I grant that the patient bites his nail, but that will not cause him to have a count of 18% eosinophiles.

Addendum: Two biopsy specimens were taken. The histological picture has been unequivocally periarteritis nodosa.

DR. S. M. BLUEFARB: This patient does have a temporal arteritis. There have recently been an increasing number of reports in the literature indicating that temporal arteritis is a manifestation of periarteritis nodosa.

DR. ZACHARY FELSHER: Periarteritis nodosa is a disease of the small vessels, while temporal arteritis is a disease of the large vessels. I think the whole diagnosis could be settled easily by biopsy of tissue from the temporal artery, because the pathologic picture of temporal arteritis is entirely different from that of periarteritis nodosa. In temporal arteritis recovery occurs within six months to a year.

Discoid Lupus Erythematosus. Presented by DR. SAMUEL J. ZAKON and (by invitation) DR. B. J. PASS.

Facial Melanosis Associated with Local Vasomotor Instability (Riehl's Melanosis?). Presented by DR. ALLAN L. LORINCZ (by invitation).

Persistent Pityriasis Rosea (?). Presented by DR. MALCOLM C. SPENCER, Danville.

Keratosis Palmaris et Plantaris. Presented by DR. S. M. BLUEFARB and DR. MALCOLM C. SPENCER, Danville.

Morphea (?), Coup de Sabre Type (?). Presented by DR. MALCOLM C. SPENCER, Danville.

Scleroderma (Two Cases). Presented by DR. DAVID OMENS and (by invitation) DR. HAROLD OMENS and DR. STEFAN BIELINSKI.

Necrobiosis Lipoidica Diabeticorum Sine Diabetes. Presented by DR. SAMUEL J. ZAKON.

Hidradenitis Suppurativa. Presented by DR. JAMES R. WEBSTER and DR. STANLEY HUFF and (by invitation) DR. J. F. SICKLEY.

Adenoma Sebaceum. Presented by DR. HERBERT RATTNER and DR. HAROLD H. RODIN and (by invitation) DR. STEFAN BIELINSKI.

Sickle Cell Anemia with "Tower Skull." Presented by DR. SAMUEL BLUEFARB and DR. AARON L. GOLDBERG and (by invitation) DR. J. F. SICKLEY.

Case for Diagnosis (Generalized Sweat-Gland Inflammation ?). Presented (by invitation) by DR. H. M. SHAIR, Quincy, at the Jan. 21, 1953, meeting.

CLEVELAND DERMATOLOGICAL SOCIETY

Herbert H. Johnson, M.D., *President*

Benjamin P. Persky, M.D., *Secretary*

Allen E. Walker, M.D., *Reporter*

Sept. 24, 1953

Granuloma Annulare. Presented by DR. JOHN E. RAUSCHKOLB.

L. C., a white retired widower, aged 52, developed a rash on the left upper arm, lateral surface, in March, 1950, one month after arriving in Japan. While en route to Japan, a rash developed on his face, which cleared up promptly on the administration of benadryl orally. While in Japan from March, 1950, to January, 1953, he was continuously under the care of the Army medical officers. Aside from the skin lesions, the entire work-up, including roentgenological, hematological and visceral examinations, showed no abnormalities.

On the upper extremities, neck-band area, chest, abdomen and back, there are lesions that are circular or oval in shape, varying in size from 1 to 2 cm. in diameter, with a hard, pearly, elevated border with an atrophic center.

A biopsy specimen, removed in Tokyo and sent to the Army Institute or Pathology for interpretation, showed findings consistent with a diagnosis of granuloma annulare, as evidenced by central coagulation necrosis of the connective tissue occurring in the upper portion of the cutis. The connective tissue degeneration was marked. Occasionally a foreign body giant cell was seen.

DISCUSSION

DR. G. W. BINKLEY: I do not think the man has granuloma annulare, because the lesions show no predilection for the extensor aspects of the joints, the color is not characteristic, and there are too many lesions on his face, neck, and trunk. The best evidence for granuloma annulare seemed to be the one histologic area which was round and which showed some necrobiosis centrally and giant cells in the periphery. In spite of the negative chest roentgenograms, the negative tuberculin, and the absence of systemic symptoms, I feel that eventually we would be able to prove sarcoidosis. I would withhold the final diagnosis in this case.

DR. E. J. ARDAY: The patient should be investigated for leprosy. There is no culture and no smear. He developed his lesions while in the Orient.

DR. G. R. STROUD: The atrophy and the telangiectasia are unusual for granuloma annulare.

DR. J. E. RAUSCHKOLB: This is one of the most remarkable cases I have ever had in my practice. I thought clinically that it was granuloma annulare. I saw one or two of those lesions on the ankles or knees, on points of pressure where he could receive trauma, and clinically I immediately thought of granuloma annulare. Because of the increased numbers of lesions, the almost generalized involvement of the torso, the upper extremities, neck, and face, and to a lesser degree the hip area, the almost massive involvement, the eruption is exceedingly extensive for granuloma annulare. Contrary to what Dr. Arday said, he did not develop the eruption

while in the Orient but on the way over, three years ago. He originally was from Kentucky. He had controlled observation by the Army doctors, either as an in- or an out-patient at the hospital in Tokyo. The biopsy sections (three in number) all show microscopically a beautiful picture of granuloma annulare. They show nothing of the characteristics of sarcoidosis. They certainly do not lead one to think that we are dealing with leprosy. He has received no therapeutic procedures from me. I still think he has a very marked case of granuloma annulare.

Purpura Annularis Telangiectodes (Majocchi). Presented by DR. JOHN E. RAUSCHKOLB.

Lupus Vulgaris with Superimposed Squamous Cell Carcinomas. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR. JOHN E. RAUSCHKOLB.

Mycosis Fungoides; Tinea Cruris; Poikiloderma Atrophicans; Cystitis. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR. JOHN E. RAUSCHKOLB.

Erythema Annulare Centrifugum (Darier). Presented by DR. JOHN E. RAUSCHKOLB.

Chronic Discoid Lupus Erythematosus with Possible Riehl's Melanosis. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR. JOHN E. RAUSCHKOLB.

Sarcoidosis and Pyelonephritis. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR JOHN E. RAUSCHKOLB.

Subcutaneous Calcinosis or Multiple Calcification of the Subcutaneous Tissue. Presented by DR. JOHN E. RAUSCHKOLB.

A Case for Diagnosis (Epidermolysis Bullosa?). Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR. JOHN E. RAUSCHKOLB.

Disseminated Neurodermatitis with Eosinophilia. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR. JOHN E. RAUSCHKOLB.

Acanthosis Nigricans. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. REES for DR JOHN E. RAUSCHKOLB.

Pseudoxanthoma Elasticum. Presented by DR. J. BEMBENISTA, DR. G. RYDER, and DR. J. Rees for DR. JOHN E. RAUSCHKOLB.

LOS ANGELES DERMATOLOGICAL SOCIETY

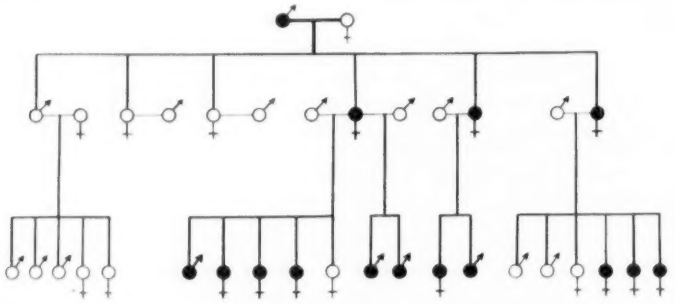
J. Walter Wilson, M.D., *President*

Anker K. Jensen, M.D., *Secretary*

Oct. 13, 1953

Keratosis Follicularis. Presented by DR. CLEMENT COUNTER.

A. W. and E. W., American girls, aged 18 and 16 years respectively, stated that the present eruption had begun during early childhood. Similar cutaneous changes were and are present in other members of the family, as noted in the accompanying diagram. Aggravation was reported on exposure to the sun.



Pedigree.

On the face, neck and extremities, as well as on the forearms and legs, typical follicular papules, forming in part confluent plaques, are present. Scattered lesions are also seen on the torso.

Microscopic examination showed the characteristic changes of Darier's disease.

Treatment has consisted of vitamin A in aqueous solution (Aquasol A), 25,000-unit capsules, twice a day, and local application of 3% salicylic acid and sulfur.

DISCUSSION

DR. A. FLETCHER HALL: I would suggest, if vitamin A therapy is given, that it be given in much larger doses. I have tried to control several cases of keratosis follicularis with vitamin A, and they usually need from 100,000 to 250,000 units a day.

DR. CLEMENT COUNTER: In the month since I first saw these patients they have improved a great deal. Largely this improvement seems to be in response to the taking of 50,000 units a day of water-soluble vitamin A. Part of the improvement present today is due to the local use of an ointment containing 3% each of salicylic acid and sulfur. My reason for presenting these patients is the preponderance of women affected by the disease as shown in the diagram, contrary to the usual statements in current textbooks. The distribution on the extremities, rather than on the trunk, is also a remarkable feature.

DR. MURRAY ZIMMERMAN (by invitation): It has been reported that oil-soluble vitamin A product is only 20% absorbed. Hence, 50,000 units of water-soluble vitamin A should be equal to 250,000 units of the oil-soluble.

Sclerosing Lipogranuloma Vs. Foreign Body Lipogranuloma. Presented by DR. V. D. NEWCOMER.

A 57-year-old American man stated that in July, 1952, a penile "ulcer" appeared following a traumatic abrasion, accompanied by painful swelling. After two injections of penicillin, the "ulcer" healed but recurred six weeks later at the same site, and it persisted. He was admitted to the Los Angeles County General Hospital, where a diagnosis of sclerosing lipogranuloma was made. The administration of cortisone caused regression of the disorder on three different occasions, but it always recurred.

The patient admitted to promiscuity and heavy consumption of alcohol but denied any act or procedure involving injections of a foreign oil into the penis or scrotum. He refused to submit to hypnosis of amobarbital (Amytal).

Physical examination reveals an indurated lobulated granulomatous mass involving the shaft of the penis. This process extends to the base of the penis, scrotum, and suprapubic area. Shotty, firm lymph nodes are palpable in the inguinal regions.

	Penile Lesion, %	Penile Controls 3 Cases, %	Inguinal Node Lesion, %
Total lipids	7.1	3.6-5.5	33.0
Total fatty acids	1.58	0.5-1.49	0.210
Total neutral fats	5.225	2.8-4.0	32.6
Total cholesterol	0.295	0.16-0.22	0.182

Repeated roentgenograms of the chest showed evidence of cavitation. Although no acid-fast organisms could be demonstrated in sputum, and animal inoculations were unsuccessful, the patient was subsequently placed on streptomycin and PAS.

Laboratory investigations, including complete studies of peripheral blood, nonprotein nitrogen, and serum protein, and urinalysis, showed normal findings. The reactions to the Frei and Ducrey tests, and to blastomycin 1:1000 were negative. The PPD first strength, showed a 3+ reaction. The coccidioidin and histoplasmin 1 and 2+ reaction. The complement fixation test for lymphogranuloma venereum was positive in serum dilutions of 1:80 on two different occasions. Four months later titer dropped to 1:20, and coccidioidin 1:2 was 4+, but negative in all other dilutions. The precipitin tests were negative.

Biopsies of penis showed a chronic nonspecific ulcer, dense hyalinizing subepidermal scarification, chronic inflammation, and small lipid droplets, accompanied by some histiocytosis. Sudan IV showed pink orange droplets, and Nile blue sulfate showed delicate pale pink. Osmic acid, no staining of droplets. Impression was that of a foreign lipid granulomatosis with nonspecific inflammation. Giemsa stain done on a section from the penis revealed no Donovan bodies. Inguinal lymph node contained sinusoidal, trapped lipid, showing no evidence of granulomatous reaction.

The lipid material extracted from the above tissue had the properties of mineral oil in that it was nonsaponifiable, oily in appearance, insoluble in cold alcohol, and insoluble in castor oil.

DISCUSSION

DR. NELSON PAUL ANDERSON: I don't believe there is a lipogranuloma of the penis or scrotum. This disorder belongs to the paraffinoma group. There is a similar case at the present time in the Naval Hospital in San Diego. These persons strike one as though they were peculiar psychologically. I think that at some time or other he has had some mineral-oil type of injections into this area.

DR. SAMUEL AYRES III: Having witnessed the remarkable improvement from the first course of cortisone therapy, I wonder if a prolonged course of cortisone would not be worth while.

DR. WALTER NICKEL: The patient mentioned by Dr. Anderson had involvement of the scrotum as well as of the penis. A plastic repair with satisfactory cosmetic result was performed.

A Case for Diagnosis. Possible Dermatitis Herpetiformis or Possible Pemphigus(?).

Presented by DR. M. E. OBERMAYER and (by invitation) DR. B. F. HARTWELL.

J. B., a man aged 68, had gastrointestinal complaints in 1952, diagnosed as chronic ulcerative colitis, treated by means of blood transfusions and short trial with cortisone. Because of edema of the right leg, the administration of cortisone was discontinued. Several days later bullae appeared on that leg and persisted.

He was seen by one of us (B. F. H.) in April, 1953, and, after conventional local therapy had proved ineffective and the eruption had spread to other parts of the body, a biopsy was performed. The features of the microscopic section were suggestive of both dermatitis herpetiformis and pemphigus.

The administration of sulfapyridine was not followed by improvement, and oxytetracycline (Terramycin) given later was equally ineffective. Following a futile trial with injections of iron, cacodylate, crude liver, and vitamin B_{12}, cortisone, 100 mg. daily, orally was added, with rapid but only partial clearing of the eruption.

Because of the continuation of his gastrointestinal complaints, a total colectomy and ileoproproctostomy was performed in July. He was prepared for the operation by the combined administration of streptomycin and penicillin, with almost complete clearing of the eruption. The pathological finding was chronic ulcerative colitis with polyposis.

The dermatitis, however, recurred soon, and was controlled only partially by the oral administration of 100 mg. of cortisone. Subsequently, extraction of two abscessed teeth was not followed by any change in the disorder.

A vesicular and bullous eruption, consisting of tense and thick-walled lesions of various sizes, is present on upper and lower extremities and the genital region. In addition, large, sharply bordered plaques, covered with serous crusts, are seen on the extremities.

Hemogram showed secondary anemia and eosinophilia. Repeated urinalyses were normal. Sedimentation rate was 46.

DISCUSSION

DR. MURRAY ZIMMERMAN (by invitation): Since the causes of dermatitis herpetiformis and pemphigus are unknown, I suggest, from the presence of bullae, pus, and eosinophiles, that as a working hypothesis we consider this patient's disease as a combination of infection and allergy, dermatitis herpetiformis being possibly such a combination. There might be two ways of treating such an eruption: one, to eliminate infectious organisms and, the other, to render the patient less allergic to them. I think it would be well to try other antibiotics, especially erythromycin (Erythrocin) and to use Staphylococcus toxoid in very high dilution to begin with. Grasping at a therapeutic straw, a trial with quinacrine (Atabrine) may also be made in line with the recent article on "Pustular Psoriasis" in the A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

DR. MILTON GOLDMAN: Questioning him, I was told that he had a severe emotional shock three years ago, and he felt that this was related to the onset of his cutaneous eruption.

DR. A. FLETCHER HALL: There are certain factors in this case that suggest impetigo herpetiformis, which is almost always associated with internal disease. The one case I reported in a man some years ago (ARCH. DERMAT. & SYPH. **50**:107-111 [Aug.] 1944) and others I

found in the literature at that time were associated with thoracic disease, and it seems to me that among these cases some were reported to have been associated with colitis. That was before the antibiotic era, so I tried all the sulfanilamides and found that sulfapyridine gave the best result, although it was not curative.

DR. ANKER K. JENSEN: In my opinion cortisone should be given in much larger doses before it is considered ineffective.

DR. LOUIS H. WINER: Histologically, I favor the diagnosis of dermatitis herpetiformis because the vesicles are subepidermal and there is a heavy eosinophilic infiltrate in the cutis. There is no lysis of epidermal cells, as one sees in pemphigus vulgaris. Clinically, however, I would favor pemphigus, and, therefore, would advise examination of a cytologic smear for Tzanck cells and another biopsy of an intact small bulla, previously frozen with ethyl chloride spray.

DR. M. E. OBERMAYER: I had the opportunity of seeing this patient in consultation. The diagnostic problem is not likely to be solved by continued histopathologic and cytologic studies, attempting to differentiate betweeen dermatitis herpetiformis and pemphigus. I do not think it is either. Pemphigus of such long and continued duration would be apt to show involvement of the mucous membranes and the intertriginous areas, neither of which are affected. I feel that perhaps we are dealing with a bullous eruption from an undiscovered, low-grade, systemic infection, viral and/or pyogenic. The large plaques with their sharply delineated, advancing borders are suggestive, and so is the fact that the eruption cleared when streptomycin and penicillin were concomitantly used in the preparation of the patient for abdominal surgery; flare, while he was on cortisone therapy, could also be interpreted in that sense. Therefore, cultured studies will perhaps shed more light on the problem and, therapeutically, the combined administration of streptomycin and penicillin in massive doses should be tried.

DR. B. F. HARTWELL (by invitation): The reaction to the potassium iodide test was negative; Nikolsky's sign was constantly absent, and the appearance of the bullae favored dermatitis herpetiformis. I doubt that repeated cytologic studies of the lesions would shed further light on the disorder. I shall follow the suggestions of the discussers.

Turban Tumor. Presented by DR. NORMAN E. LEVAN.
Xanthoma Tuberosum of the Palms. Presented by DR MILTON GOLDMAN.
Lichen-Like Linear Nevus. Presented by DR. ANKER K. JENSEN.
Nevus. Presented by DR. WALTER R. NICKEL.
Granuloma Annulare. Presented by DR. J. WALTER WILSON.
A Case for Diagnosis: Disseminated Lupus Erythematosus(?). Presented by DR. KENNETH L. STOUT.
A Case for Diagnosis: Scleroderma or Lichen Sclerosis(?). Presented by DR. FLETCHER HALL.
Dermatitis Herpetiformis. Presented by DR. LAWRENCE M. NELSON.
A Case for Diagnosis: Connective Tissue Nevus(?). Presented by DR. KENNETH L. STOUT.
Generalized Scleroderma with Bleb Formation and Alopecia Universalis. Presented by DR. HAROLD PRICE.
Parapsoriasis (Pityriasis Lichenoides et Varioliformis Acuta?). Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Mildred Ryan, M.D., President

Joseph Goodman, M.D., Secretary

Oct. 7, 1953

Purpura Annularis Telangiectodes (?). Presented by DR. LEON REZNICK and DR. MAURICE M. TOLMAN, Boston.

M., a 33-year-old Italian-American leather worker, has had an eruption for two years in the bathing-trunk area. The lesion starts as an area of erythema, a few millimeters in diameter, which then grows to a size of 1 cm. or more, becoming slightly scaly and raised. Soon the center fades to brown, while the periphery shows a collarette of tiny, erythematous papules. Eventually, the papules also fade, the whole process taking about four weeks. The patient presents lesions in all stages of development.

Biopsy showed chronic inflammatory changes, with a patch of infiltrate in the upper corium.

DISCUSSION

DR. ALFRED HOLLANDER, Springfield, Mass.: I would like to propose a diagnosis of lichen planus annularis, although the histological specimen I saw is not compatible with that diagnosis.

DR. WALTER F. LEVER, Boston: I agree with the thesis of Randall, Kierland, and Montgomery (A. M. A. ARCH. DERMAT. & SYPH. **64**:177, 1951), according to which these authors suggest the abolition of the rather artificial separation of the four diseases: purpura annularis telangiectodes, progressive pigmentary dermatosis, pigmented purpuric lichenoid dermatitis, and angioma serpiginosum. These are all chronic, progressive, purpuric eruptions without systemic manifestations. In one of them, the pigmented purpuric lichenoid eruption of Gougerot and Blum, one finds papular lesions, and I suspect that this case represents that variant of chronic purpuric eruptions.

DR. CHESTER N. FRAZER, Boston: It seems possible that the lesions are caused by a peripheral vasculitis.

DR. ARTHUR S. SPANGLAR, Boston: I suggest that this may be a pigmented type of scleroderma.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. MILTON E. HELMAN, Boston.

E. C., a 63-year-old white housewife, noted skin lesions on the shins about six years before presentation. The lesions had slowly increased in size and number. There was no family or past history of diabetes.

Examination revealed large, sharply demarcated, yellowish patches on the shins. The central portions of the lesions are shiny and atrophic. The borders are firm and elevated and show telangiectasia.

Fasting blood sugar was 129 mg. per 100 cc.; on repeat it was 96 mg. per 100 cc. Urine examinations showed no sugar. Biopsy showed changes consistent with necrobiosis lipoidica diabeticorum.

DISCUSSION

DR. BERNARD APPEL, Lynn, Mass.: My impression is that this patient presents an extensive granuloma annulare. I have two reasons for this impression. One is the thickened, raised, uniformly wide border which completely encircles the entire lesion, and the other is the relative symmetry. I cannot recall seeing lesions of necrobiosis as symmetrical as presented in this case, although I have seen them bilaterally.

DR. ALFRED HOLLANDER, Springfield, Mass.: I believe there is a definite differential diagnostic sign between granuloma annulare and necrobiosis. In granuloma annulare there is a very definite border consisting of closely grouped nodules. In necrobiosis, as well as in porokeratosis, there is a limiting hard wall which can easily be palpated and separates the lesion from the surrounding normal tissue.

I think there is no question that we are dealing with a case of necrobiosis.

DR. E. MYLES STANDISH, Hartford, Conn.: I believe that in some of the lesions the well-demarcated border has disappeared; there is a grading off into the skin without that dusky red border which usually is seen in necrobiosis lipoidica. It is not unusual to have lesions bilaterally in exactly that same position. In every other aspect, the clinical signs fit very well with the diagnosis of necrobiosis, that is, central atrophy, pale lemon color with the blood vessels showing through, and dark purplish, reddish border.

What to do about these lesions is a problem. Some lesions have been skin grafted with excellent success, but that would be quite an extensive operation in this case. It is noteworthy that there are more and more cases being recorded in which there is no history of diabetes, in which diabetes does not develop, and in which not only the fasting level of the blood sugar but also the sugar tolerance test is entirely normal. It has been suggested that we omit the "diabeticorum" part of the name in the case of those that are not diabetics.

DR. WALTER F. LEVER, Boston: I want to stress the fact that the majority of patients with necrobiosis do not have lipid infiltration in the lesions. In recent years, I have found hardly any case of necrobiosis in which I could demonstrate lipids in the sections.

Granuloma. Presented by DR. BERNARD APPEL, Lynn, Mass.

S. B., a 28-year-old white housewife, developed an itching eruption on the right leg about nine months before presentation. The lesion started as a red papule which gradually enlarged, forming an annular lesion.

Examination revealed a lesion, about 6 by 10 cm., on the anteromedial aspect of the right leg just below the knee. The lesion is made up of a smooth, flat central zone, surrounded by crusted, bluish-red papules.

Cultures for fungi were repeatedly negative until a culture was done from material removed for biopsy. The cultural findings after one week suggested that the organism is Trichophyton rubrum.

DISCUSSION

DR. JACOB H. SWARTZ, Boston: This is a very interesting case. It reminds me of Dr. Walter Wilson's cases in "Nodular Granulomatous Perifolliculitis of the Legs Caused by Trichophyton Rubrum" reported at the last meeting of the American Dermatological Association. The perifollicular involvement, the development of granulomatous lesions within the confines of a scaly erythematous plaque, the sex, the location, and the culturing of a fungus from the biopsy tissue are all in favor of this case resembling Wilson's reported cases.

I would like to see the culture from the biopsy specimen. I would also like to see the biopsy tissue stained by the Hotchkiss-McManus method, since the fungus cannot be easily detected with the usual tissue stains.

DR. OTIS F. JILLSON, Hanover, N. H.: This is an excellent example of granuloma produced by Trichophyton rubrum. These nodular lesions occurring in women who shave their legs came into being when Mescon and Kligman stressed the importance of the periodic acid-Schiff stain for the demonstration of fungi.

The spores of Trichophyton rubrum are not visualized when routine H and E stains are employed. It is necessary to use the P. A. S. stain to show these large spores in the corium.

If you take some purulent material from one of the follicular lesions and clear this material with potassium hydroxide, you will very frequently find clusters of large spores. It is freqently necessary to culture not the scales but this purulent material or to do a biopsy and culture this material.

DR. ROBERT F. TILLEY, Brookline, Mass.: I think the diagnosis of lupus vulgaris should also be considered in this case. In addition to the skin lesions on the legs, the patient has on the right side of the neck a scar which has been present since childhood. This is consistent with scrofuloderma.

Discoid Lupus Erythematosus (?). Presented by DR. MAURICE K. TOLMAN, Boston.

B. K., a 36-year-old white male baker, developed slightly itchy, raised red lesions on the back of the neck about six months before presentation. Six weeks before presentation, similar lesions appeared on the face and forehead.

Examination revealed sharply demarcated, raised red lesions, 1 to 3 cm. in diameter, on the areas mentioned above. Chest x-ray was negative. Biopsy showed acanthosis, with chronic inflammation.

Treatment with sulfisoxazole (Gantrisin) and oxytetracycline (Terramycin) orally had resulted in no appreciable change.

DISCUSSION

DR. MYLES STANDISH, Hartford, Conn.: Clinically the findings fit in fairly well with the diagnosis of discoid lupus erythematosus. The eruption is rather extensive for the short duration. There are lesions on the lobes of the ears, but I could see none in the concha or in the mouth. Some of the lesions are indurated and show indications of abscess formation, the "profundus" type of lupus erythematosus.

This should be a good case for treatment with chloroquine (Aralen) phosphate. Of 10 cases of not quite as severe a type and 1 severer case which I treated with Aralen, 3 cases cleared

up entirely. I gave the patients two tablets a day for about a week, reducing the dose then to one tablet a day. Some of the cases have been entirely in remission now for as long as two or three months.

One man with lupus erythematosus of 10 years' duration had had several courses of bismuth and gold. Quinacrine (Atabrine) hydrochloride also had failed to control the process. On treatment with Aralen there was marked improvement.

The most striking result was obtained with a patient who appeared to be going into acute dissemination three years ago. There was leucopenia and a tendency to reversal of the albumin-globulin ratio. Treatment consisted of fairly large doses of cortisone. At the end of 10 days the dose was reduced to 100 mg. daily. On deciding to leave the hospital against advice the patient was told to stop taking cortisone, but she continued to take 100 mg. a day for two years. At the end of that period, she was found to be completely normal, except for the lupus which was unchanged. After she was given Aralen, all signs of activity of the lupus erythematosus disappeared promptly.

DR. JACOB H. SWARTZ, Boston: Before treatment is started with Atabrine, I should like to suggest that the diagnosis of sarcoid be ruled out. The lesions are variable. Most of them are granulomatous. In my experience, lupus erythematosus profundus is not as extensive, and the sites of predilection are the lower lip, sides of the mouth, and the chin. Cases in which lupus erythematosus and sarcoid are associated have been reported.

Chronic Discoid Lupus Erythematosus. Presented by DR. JULIUS PICARD, Fall River, Mass.

B. N. a 40-year-old American fireman, four months before presentation developed an eruption on the nose, on the lower lip, and about the ears. The lesions, up to 2 cm. in diameter, are red, scaly, and elevated. Some show atrophy. The lower lip is diffusely dry and scaly and somewhat swollen.

Chloroquine (Aralen) phosphate has been given intermittently from July to September, with marked improvement.

DISCUSSION

DR. JOHN L. FROMER, Boston: We have treated some 18 patients with either chloroquine (Aralen) or quinacrine (Atabrine). The course of the disease in these patients is by no means uneventful. Two patients have developed depression of bone marrow. Some patients cannot tolerate either chloroquine or quinacrine. Two patients who were treated with both improved more with quinacrine.

Finally, I wish to point out that the verrucous variety of lupus erythematosus responds better than the banal flat type.

DR. ALFRED HOLLANDER, Springfield, Mass.: I think that a peculiar attitude has developed among physicians during the last few years about treatment in general. It appears that as soon as a new treatment is found old reliable drugs are often discontinued and the new drug, which was introduced without rationale, is used exclusively. Gold is still good therapy for lupus erythematosus. Many patients may benefit from Atabrine, Aralen, gold, and/or other therapeutic agents; others may not benefit from any therapy. I feel that all of us should use more critical judgment in carrying out treatment on our patients. Cases of chronic discoid lupus erythematosus which show good scarring and no active symptoms at all do not need any treatment.

DR. WALTER F. LEVER, Boston: I think that Dr. Hollander's remarks are well taken. However, I believe they should not apply to the use of chloroquine (Aralen) in the case of patients with discoid lupus erythematosus. I would say there has not been any treatment as effective as chloroquine. I had quite a backlog of patients with chronic discoid lupus erythematosus who had received long courses of bismuth and gold with improvement that was only slight if at all. Every one of them responded favorably to chloroquine. The improvement comes usually within the first few weeks and then levels off. Most patients who have long-standing and severe lupus erythematosus do not clear up entirely. Those with milder cases often do. So far, there has been no drug for chronic discoid lupus erythematosus as satisfactory and as safe as chloroquine. The danger of side-reactions is far less than with gold.

DR. MAURICE M. TOLMAN, Boston: There are certain types of lupus erythematosus that will respond to most anything, and then there are other types that just resist everything. But nothing has given as quick and satisfactory responses and relatively good results in a short time as have quinacrine (Atabrine) and certainly chloroquine.

Benign Mucous Membrane Pemphigus. Presented by ARTHUR S. SPANGLER, Boston.

E. R. C., a 55-year-old white housewife, had had areas of alopecia on the scalp and tender erosions of the gums for two and one-half years. Biopsy of a scalp specimen showed a subepidermal bulla.

The patient received corticotropin gel in a dose of 80 units a day for three weeks. Treatment was stopped three months ago, because the patient developed a psychosis. There have been no new lesions since the treatment was stopped.

DISCUSSION

DR. WALTER F. LEVER, Boston: This patient has the disease originally described as ocular pemphigus but better designated as benign mucous membrane pemphigus, because a good percentage of these patients do not ever have any ocular involvement.

It is characteristic of this disease that it is benign, that it is chronic, and that the lesions frequently heal with scarring. The lesions are most commonly present on the mucous membranes, particularly the conjunctivae, but in about one-third of the patients cutaneous lesions are found. The cutaneous lesions may occur as discrete vesicles, but more often they occur as persistent erythematous areas, with recurring flaccid bullae which finally heal with scarring. The scalp is one of the most commonly involved areas, as well as the side of the face.

When this patient was first seen by Dr. Spangler and me, she had active lesions on the gums and on the scalp. On the gums vesicles were present, but on the scalp there were none. However, the biopsy specimen which was obtained at that time from the scalp and which is presented today showed extensive detachment of the epidermis from the underlying dermis. That is characteristic of this disease which has subepidermal bullae without acantholysis.

The response to corticotropin certainly was very gratifying.

The biopsy specimen was taken from the scalp. The patient has erythematous crusted lesions throughout the scalp. They now have all healed with atrophy, which is characteristic of benign mucous membrane pemphigus.

These scars are atrophic, and the follicles are destroyed. On several occasions, cases like this one with oral and scalp lesions have been presented at Society meetings as instances of lupus erythematosus. Of course, once atrophic scarring has taken place, there is no way of differentiating the lesions from other lesions ending in atrophy.

Generalized Exfoliative Dermatitis (Mycosis Fungoides?). Presented by DR. JULIUS PICARD, Fall River, Mass.

C. S., a 69-year-old retired Italian-American millhand, developed generalization itchiness without skin lesions seven years before presentation. In the three years before presentation, scaling and redness of the skin developed. From time to time, small infiltrated areas appeared in the skin. Biopsy showed changes consistent with but not characteristic of mycosis fungoides. Many local treatments and arsenicals by mouth were without effect.

DISCUSSION

DR. BERNARD APPEL, Lynn, Mass.: My impression is that this patient's disease definitely belongs to the group of the chronic lymphogranulomatoses. Although the progress of the condition and its resistance to radiation therapy are somewhat against the diagnosis, there are certain changes histologically which make me feel that it should be classified as mycosis fungoides. This is principally because of the beginning disorganization of the architecture of the basal layer of the epidermis in some locations, the infiltrate which is polymorphic to some extent, although predominantly of the lymphatic type, and the general clinical impression.

DR. CHESTER N. FRAZIER, Boston: It seems to me that before a diagnosis of mycosis fungoides can be made there must be more evidence than we have at present. The fact that this patient has a chronic exfoliative dermatosis does not necessarily mean that he has a lymphoma. I think a diagnosis of lymphomatous disease of the skin cannot be made without histological evidence of it.

DR. JULIUS PICARD, Fall River, Mass.: The opinions of histopathologists who saw the slide were in disagreement as to diagnosis. Clinically the case suggests mycosis fungoides. The main complaint of this man is now uncontrollable itching of the skin.

DR. JACOB H. SWARTZ, Boston: I am glad Dr. Frazier brought up that point. Time and again the same issue comes up. Exfoliative dermatitis and lymphadenopathy do not necessarily substantiate a diagnosis of mycosis fungoides. A blood picture of 36% lymphocytes and 6% eosinophiles simply means that this man has a chronic pruritic dermatitis. The burden of proof is on the one who calls it mycosis fungoides. It is true that 1 or 2 patients, out of 10 patients with such a picture, may develop infiltrated lesions and tumors, with a histopathologic picture of mycosis fungoides, but the other 8 or 9 patients never do.

DR. JOHN L. FROMER, Boston: We have now treated 14 patients with proved mycosis fungoides with cathode rays. Although this is an extremely useful medium, we are still very cautious about the type of patient that we are accepting and, more particularly, the appearance of the peripheral blood and sternal marrow.

I should like to comment on some of these patients, because it has some bearing on the patient we are discussing. Three proved cases of mycosis fungoides have had repeated negative biopsies over a period of years. We have seen a patient with proved mycosis fungoides in whom the tumor stage yielded a negative biopsy. Nonetheless, a diagnosis of mycosis fungoides requires a pathologic picture of characteristic changes to support it.

During the past year we have treated four patients with either exfoliative dermatitis or generalized dermatitis of unknown etiology, who have been resistant to all the usual therapies, including corticotropin. The patient has gone into a remission in each case in response to cathode-ray therapy.

DR. WALTER F. LEVER, Boston: I should like to make two points. First, in regard to diagnosis, I agree with those who say that the only diagnosis we can make here is that of a generalized exfoliative dermatitis. We know well that generalized exfoliative dermatitis can be either idiopathic or symptomatic. One of the symptomatic causes of generalized exfoliative dermatitis is lymphoma. In the initial period, the number of lymphoma cells can be very small and these cells are then difficult to discover, but until they are discovered by repeated biopsies, we should not make a diagnosis of lymphoma. Montgomery (A. M. A. ARCH. DERMAT. & SYPH. **27**:253, 1953) states that about 25% of patients with generalized exfoliative dermatitis ultimately turn out to have lymphoma.

The second point that I should like to make is in regard to therapy. I think we need to do something about this patient. He is desperate. My experience with cathode rays is not extensive, but I would say that this treatment has its hazards. We have had several patients here at the Massachusetts General Hospital who did not do well with it. There is the danger of bone marrow depression. My suggestion is that the patient receive oral cortisone, starting with 200 mg. a day for three days, followed by 150 mg. a day for three days, and then being given 100 mg. a day for a long time. This amount is not going to clear up his skin entirely, but it probably will give him considerable relief from his severe itching. Doses of cortisone of 100 mg. a day are generally safe to give, provided that the patient is under observation.

Tinea Capitis in a Sixteen-Year-Old Male Caused by Microsporum Audouini. Presented by DR. MAURAY J. TYE, Haverhill, Mass.

Scleroderma (Two Cases). Presented by DR. MAURICE M. TOLMAN, Boston.

Psoriasis? Parapsoriasis. Presented by DR. LEO KORETSKY, West Medford, Mass.

Lichen Pano-Pilaris?. Presented by DR. ROBERT H. GOLDFARB, Boston.

Morphea Type of Basal Cell Epithelioma. Presented by DR. WALTER F. LEVER, Boston.

Scleroderma. Presented by DR. MAURICE M. TOLMAN and (by invitation) DR. JOHN H. COX, Boston.

Granuloma Annulare?. Presented by DR. MILTON E. HELMAN, Boston.

Schamberg's Progressive Pigmentary Dermatosis. Presented by DR. WILLIAM J. MACDONALD, Boston.

Granuloma Annulare. Presented by DR. WILLIAM J. MACDONALD, Boston.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Bertram Shaffer, *Chairman*

Lewis M. Johnson, M.D., *Secretary*

October 16, 1953

Nevoid Growth (?). Presented by DR. JOHN P. SCULLY, Reading.

D. W., a white boy, aged 2 years, presents a number of slightly raised, yellowish plaques confined to the right thigh. They are somewhat linear, tumescent, raised, yellowish plaques with a slightly pigskin-like surface extending about 3 by 4 fingerbreadths over the lateral surface of the right thigh.

The parents have noted the process from birth. The lesions are asymptomatic and apparently have not changed materially. The child is normal in development and has had no serious illnesses.

The report of the biopsy specimen was as follows: "The architecture of this specimen of skin had not been particularly disturbed except in the center of the section where there had been some compaction of the fibrous tissue and the fat was seen high in the dermis. The epidermis was within normal limits and there was no inflammatory reaction" (Dr. Herman Beerman). Pathological diagnosis: Collagenous plaque(?).

DISCUSSION

DR. JOHN P. SCULLY, Reading: I am considering the diagnosis of tuberous sclerosis, and I am particularly anxious to hear what Dr. Butterworth has to say about this diagnosis.

DR. THOMAS BUTTERWORTH, Reading: This picture is consistent with the plaques seen in tuberous sclerosis. The child has no symptoms or other signs of that disease but, as I have stated before, I have had the experience of observing patients with plaques develop subsequent adenoma sebaceum. Therefore this child will bear watching. Thus far, he walked at 10 months, talks quite well, and there is nothing to indicate tuberous sclerosis. However, it is not unusual for these children to progress normally up to about the fifth or sixth year, when they begin to fall behind. I suggest, therefore, that Dr. Scully check this child after 6 or 12 months and be on the lookout for other signs of that disease, talk and play with the child, and try to get some comprehension of his accomplishments from a mental point of view.

Keratoacanthoma. Presented by DR. BERTRAM SHAFFER, DR. HERMAN BEERMAN and (by invitation) DR. EDWIN J. LEVY, and DR. MILTON M. CAHN.

M. F., a white woman, aged 38, of good general appearance, presented a 1-cm. hemispherical nodule, firm, skin-colored, with a central crater filled with keratinous material, located on the left nasolabial fold.

The patient was first seen on June 6, 1953. At that time she gave a history of a small papule which started about four to five weeks previously and had rapidly enlarged to its present size. A biopsy was done on June 15, 1953. The lesion rapidly regressed, and had completely disappeared by July 28, 1953. Only the biopsy scar remained.

The report on the biopsy specimen was as follows: "This section showed marked hyperkeratosis forming a keratin plug overlying an area of invaginated epithelium. There were some areas of parakeratosis. There was marked acanthosis with atypical prickle cells with hyperchromatic nuclei." Diagnosis from biopsy specimen: "Senile keratosis with squamous cancer change."

DISCUSSION

DR. MILTON M. CAHN (by invitation): Dr. Levy and I, while at the Skin and Cancer Hospital of Philadelphia, saw several of these cases which showed histologic features resembling senile keratosis with squamous cell epithelioma. At that time Dr. John B. Lyon of the Westminster Hospital, London, England, was here as a visiting Fellow and he told us that in Europe they see many of these cases and have been bold enough to let them alone, and they have spontaneously disappeared. This information is contained in articles published in 1950 by Rook and Whimster (Rook, A. J., and Whimster, I. W.: Le kérato-acanthome, *Arch. belges.*

dermat. et syph. **6**:137-146 [Sept.] 1950), and by Gordon, H.: Spontaneous Resolution of Molluscum Sebaceum, *Proc. Roy. Soc. Med.* **43**:838-839 [Nov.] 1950). The condition was originally described in 1936 as "molluscum sebaceum" (MacCormac, H., and Scarff, R. W.: Molluscum Sebaceum, *Brit. J. Dermat.* **48**:624-626 [Dec.] 1936), but Rook and Whimster decided a better term would be keratoacanthoma. As you saw in the picture, it is clinically a hemispherical nodule resembling a giant molluscum or rodent ulcer or squamous cell epithelioma. However, it is benign and will disappear spontaneously. We had another patient on whom the lesion disappeared spontaneously in six weeks without any scar remaining. We feel that this is a distinct entity which can be recognized clinically. Histologically one would be bound to make the diagnosis of senile keratosis with early squamous cell epithelioma (Grade I).

DR. HERBERT LEAVITT, Easton: What clinical features enable one to recognize this condition, so that one will be bold enough to let it alone?

DR. MILTON M. CAHN (by invitation): It is a nodular cutaneous lesion, which reaches its maximum size in four or five weeks; it is a rapidly growing lesion. We have not followed any patient without taking a biopsy specimen.

DR. JACK WEINER: There is a history of three or four weeks' duration from the time of onset to its present size. On the histologic section there is a report of senile keratosis with suspicious or beginning epitheliomatosis. These two features, rapid growth clinically and very low-grade changes histologically, are incompatible. I think that is the typical feature.

DR. ALBERT M. KLIGMAN: This is a good reason for reading the foreign literature. I saw five or six of these cases in Europe last year and every time I came up to it, I had no idea what it was.

DR. CARROLL S. WRIGHT: I missed this reference in the literature completely and am sure that if I had seen the growth I would have taken it entirely out, thinking it was an epithelioma. I think it is a tribute to the presenters to recognize that it was not an epithelioma.

DR. JOHN P. SCULLY, Reading: About two years ago I had an elderly patient who developed multiple lesions over a period of six months. The original lesions was reported as early squamous cell epithelioma and was treated as such with roentgen rays, but even as I was treating that, the others appeared, and I began to feel there was something curious about it, because I had never seen multiple epitheliomata like that of the squamous cell type, so I let them alone, and they disappeared.

DR. HERMAN BEERMAN: I saw some of these patients in London and the lesions looked exactly like epitheliomas. One has, therefore, the right to consider them as such except for one thing, namely, that they are self-healing. Dr. Witten of New York has described a patient with many lesions which everyone called multiple squamous cell cancers. One also wonders whether the sunlight keratoses of Poth are not the same as keratoacanthoma.

DR. ALBERT M. KLIGMAN: There is a familial type of spontaneously involuting squamous cell carcinoma; it is rare, but it does occur. So involution does occur spontaneously in cancer.

Mycosis Fungoides. Presented by DR. M. H. SAMITZ and (by invitation) DR. FREDERICK URBACH.

C. W., a white man, aged 43, developed a pruritic, lichenoid, chronic dermatitis about 10 years ago while serving with the U. S. Armed Forces in the Pacific. Since then, the eruption has gradually extended, being primarily a scaling, erythematous, eventually infiltrated, and highly pruritic dermatitis. About two years ago he developed a generalized erythroderma. About one year ago typical tumor lesions appeared over the trunk, legs, and chest. The lesions regressed completely after cathode ray treatment, and are now recurring.

There is a patchy, erythematous, slightly infiltrated dermatitis of the trunk, arms, and legs. Some hyperpigmentation remains from the roentgen-ray therapy.

A complete hematological study on several occasions was within normal limits. The total protein, albumin-globulin ratio, serum and glucose determinations were within normal limits.

Ten biopsy specimens, taken over an eight-year period, were variously reported as neurodermatitis, nonspecific dermatitis, lichen planus, and, finally, for the past two years, as diagnostic of mycosis fungoides.

Local therapy produced no result. Five micrograms of P^{32} was given, with no result. Nitrogen mustard also did not help. Triethylene melamine and antimony given intravenously had no result. Under cathode ray therapy, 900 r to total body surface, there was complete remission. Under no subsequent treatment, there has been gradual recurrence of the lesions in the past two months.

DISCUSSION

DR. FREDERICK URBACH (by invitation): This patient was presented to the Society last year. His appearance is strikingly different now. He has had a generalized erythema for seven years, and about eight months ago developed some very large, fungating tumors on the legs, particularly around the toes, on the arms and on the trunk. He has been treated with roentgen rays, a small amount of P^{32}, arsenic, antimony and many local preparations with no very great improvement except on corticotropin, when the itching subsided. However, while he was under corticotropin therapy he developed so much water retention that we had to discontinue it. He was sent to the Lahey Clinic for a course of cathode ray therapy. This consists of a cyclotron hooked up to an x-ray machine, and cathode rays are actually emitted. This type of radiation, with a relatively low penetrating value, has been used to spray the entire body surface of this man. He has had a total dose of 900 rep. The results were almost miraculous. The patient became totally asymptomatic, the lesions disappeared, and for the first time in 10 years he has no itching. Today, three months, after therapy, he shows some recurrences, which we plan to treat with Chaoul type therapy. While experimental and expensive, this therapy has been well worth while, from the standpoint of relief to the patient. He has been able to work again. He is a young man and the prognosis is still guarded. The patient is presented to show the extraordinary effects of high-voltage cathode ray therapy on generalized lymphomas such as mycosis fungoides.

Coup de Sabre Type of Linear Scleroderma. Presented by DR. JOHN P. SCULLY, Reading.

P. A. Z., a white girl, aged 2½ years, at birth was said to have presented a reddish "V"-shaped mark just to the right of the midline of the forehead, with the apex of the "V" over the inner aspect of the right eyebrow. The redness is said to have faded after one year, and as the child has grown, there seems to have been delayed bony development beneath the area of skin involvement, and as the reddish discoloration has faded, there has been a gradual change to a whitish, sclerotic-appearing skin.

The patient is presented for discussion of prognosis. Further development of asymmetry of the face is feared.

DISCUSSION

DR. JOHN P. SCULLY, Reading: I think there is beginning hemiatrophy now.

DR. M. H. SAMITZ: If there is a sclerodermatous element, I suggest the use of chloroquine. We have followed six cases for a little over a year; three cases of scleroderma, two cases of morphea, and one of acrosclerosis. The response of some of the cases to chloroquine has been amazing.

Interim report by Dr. John P. Scully, Nov. 20, 1953: "This patient has improved clinically in the past month on chloroquine therapy."

Lichen Sclerosus et Atrophicus. Presented by DR. M. H. SAMITZ and (by invitation) DR. A. MILLER.

V. J., a white woman, aged 54, presents over the right shoulder a group of a dozen small, discrete, flat, papular and atrophic lesions with a shiny white surface with a central dell. A similar group of lesions is seen in the left clavicular region. On the lateral areas of both breasts are similar, but larger, lesions. A small group of lesions is seen over the lower abdomen, just above the pubic area. This atrophic patch probably represents the coalescence of several original papular lesions. In the vulvar area, just above the clitoris, is a small, irregular, white, atrophic patch with central delling. The patients states that this area is pruritic.

She has had no serious medical or surgical illnesses. She has had recurrent attacks of nummular eczema of both hands for the past five years. Five years ago she first noticed a

group of lesions over both anterior shoulder areas. They produced no discomfort. Three years later, similar lesions appeared on both breasts and near the intermammary cleft. About one year ago she noticed a new lesion over the lower abdomen.

All routine laboratory studies were within normal limits.

The report on the biopsy specimen was lichen sclerosus et atrophicus (Dr. Herman Beerman).

DISCUSSION

DR. JOHN P. SCULLY, Reading: Dr. Samitz will recall last spring suggesting chloroquine for lichen sclerosus et atrophicus, and since that discussion I have employed that drug in two patients. I think it is remarkable what it has accomplished. One of the patients, an Italian woman whom I presented before this Society in the middle of last winter, has since developed a remarkable involution of some of the lesions, with complete relief of itching. Another, an 11-year-old girl who has the process on the vulva, has relief of the itching for the first time, and recently that peculiar glossy-white picture of the mucosal surface which these lesions present has begun to disappear.

Mycosis fungoides (P^{32} Therapy). Presented by DR. M. H. SAMITZ and (by invitation) DR H. BOGAERT.

Ulcus Vulvae Acutum. Presented by DR. JACK WEINER and (by invitation) DR. H. POMERANTZ.

Pemphigus Erythematosus (Senear-Usher Syndrome). Presented by DR. M. H. SAMITZ and (by invitation) DR. A. B. MILLER.

Mycosis Fungoides. Presented by DR. M. H. SAMITZ and (by invitation) DR. E. D. MONTERO.

Mycosis Fungoides. Presented by DR. M. H. SAMITZ and (by invitation) DR. A. B. MILLER.

Calcification in Association with Possible Scleroderma. Presented by DR. M. H. SAMITZ and (by invitation) DR. H. BOGAERT.

Necrobiosis Lipoidica. Presented by DR. M. H. SAMITZ and (by invitation) DR. E. D. MONTERO.

Lichen Nitidus. Presented by DR. M. H. SAMITZ and (by invitation) DR. E. D. MONTERO.

Lichen Nitidus. Possible Lichen Planus(?). Presented by DR. JOHN M. SIEGEL and (by invitation) DR. H. BOGAERT.

Schamberg's Progressive Pigmentary Dermatosis. Presented by DR. M. H. SAMITZ and (by invitation) DR. A. B. MILLER.

Purpura Annularis Telangiectodes. Presented by DR. JACK WEINER and (by invitation) DR. H. BOGAERT.

Chronic Discoid Lupus Erythematosus Showing Predilection for Mucosal Surfaces. Presented by DR. JACK WEINER and (by invitat on) DR. E. D. MONTERO and DR. D. J. MADDEN.

Lupus Erythematosus. Presented by DR. M. H. SAMITZ and (by invitation) DR. H. BOGAERT.

Leukoderma Syphiliticum Appearing Ten Weeks After Apparently Curative Treatment of Secondary Syphilis. Presented by DR. IRA L. SCHAMBERG.

Kaposi's Hemorrhagic Sarcoma. Presented by DR. M. H. SAMITZ and (by invitation) DR. A. B. MILLER.

Abortive Herpes Zoster (Necrotic) with Varicelliform Eruption. Presented by DR. REUBEN FRIEDMAN.

News and Comment

GENERAL NEWS

Specialists Certified by the American Board of Dermatology and Syphilology, Inc.—As a result of its recent examinations, the American Board of Dermatology and Syphilology, Inc., has certified the following 52 physicians up to and including Dec. 31, 1953:

Robert L. Akin, Knoxville, Tenn.
Gustave T. Anderson, Portsmouth, Va.
Joseph Andrei, New York
Charles J. Balogh, Minneapolis
Sherwood W. Barefoot, Greensboro, N. C.
Adolph H. Bleier, Chester, Pa.
Patrick N. Brown, Cheshire, Conn.
Frank M. Castiglione, Hamden, Conn.
George W. Crane Jr., Durham, N. C.
Julius L. Danto, Vancouver, B. C., Canada
Bruce V. Drowns, Kansas City, Mo.
John C. Farrell, Sacramento, Calif.
Joel C. Fink, Fort Knox, Ky.
David W. Folan Jr., Boston
William B. Gibson, Media, Pa.
Eugene J. Gillespie, Stapleton, N. Y.
Victor C. Hackney, Pasadena, Calif.
James R. Hamilton, Nashville, Tenn.
Oscar E. Heim Jr., Philadelphia
Louis D. Hoffstein, Philadelphia
Samuel H. Horton Jr., Charleston, S. C.
Roland W. Jones, Indianapolis
William C. King, Austin, Texas
Ivan W. Kuhl, Fort Bliss, Texas
Morris J. Lipnik, Detroit
James H. Lockwood, San Diego, Calif.
Robert E. Lyons, San Antonio, Texas
Sheldon L. Mandel, Minneapolis
Thomas W. Moffatt, Denver
James F. Morrell, Newport, R. I.
Samuel L. Moschella, Levittown, N. Y.
John L. Mulherin, Philadelphia
Woodrow W. Murphy, Parma Heights, Ohio
Stephen R. Phelps, South Bend, Ind.
George F. Pinne, Omaha
Robert H. Preston, Cincinnati
Christian E. Radcliffe, Iowa City
Saul Rosenberg, Bridgeport, Conn.
Samuel Schwebel, Youngstown, Ohio
Michael J. Scott, Seattle
James C. Sisk, Kirkwood, Mo.
Edwin A. Smith, Lynn, Mass.
Frederick Urbach, Philadelphia
Cornelius A. Vander Laan, Chicago
Sanford M. Vaughan, San Antonio, Texas
Alan D. Watson, Kent, Conn.
Edward W. Wilson, New York
Wayne L. Wright Jr., Mare Island, Calif.
Joel W. Wyman, Anderson, S. C.
Stanley N. Yaffe, Baltimore
Louis Yates, Merion, Pa.
Frederick B. Zaugg, Coral Gables, Fla.

The following 53 dermatologists also passed the examinations, and will be certified upon fulfillment of other requirements:

Milo O. Blade, Falls Church, Va.
Harry Boatwright, Camp Lejeune, N. C.
Donald G. W. Brooking, Decatur, Ala.
Alfred B. Brotman, Oceanside, N. Y.
Charles W. Caccamise Jr., Jackson, Miss.
Warren Smoot Carter, Winchester, Va.
Donald P. Cole Jr., Hanover, N. H.
John M. Coletti, Salt Lake City
Frank W. Crowe, Boise, Idaho
Thomas L. Day, New York
Raymond J. Dempsey, Joliet, Ill.
Richard N. Duffy Jr., Knoxville, Tenn.
Leah Fisher, Chicago
Alvo A. Guiducci, Warren, Ohio
C. G. Harner, Columbus, Ohio
Homer E. Harris Jr., Chicago
William J. Hemphill, Eugene, Ore.
Mark B. Hollander, Baltimore
Coleman Jacobson, Philadelphia
Royal G. Jennings, High Point, N. C.

Jerome Kimmelman, Brooklyn
John D. Krafchuk, Minneapolis
Wilfred H. Kurashige, Honolulu, T. H.
Ralph Langer, Brooklyn
M. Paul Lazar, Highland Park, Ill.
S. William Levy, San Francisco
Irwin H. Linden, Los Angeles
Carl E. Lipschultz, % Postmaster, New York
Jacob S. Ludwig, York, Pa.
William S. Maddin, Vancouver, B. C., Canada
John C. Massar, Portland, Ore.
P. Michaelides, New York
Michael J. Mitchell, Ambridge, Pa.
Calvin C. Mitchener, Raleigh, N. C.
Miriam Reed, Princeton, N. J.
Bernard L. Rhodes Jr., San Francisco
Lyon Rowe, Los Angeles
John Paul Ruppe Jr., Islip, N. Y.
Philip E. Schwartz, Portland, Conn.
Paul O. Shackelford, Henryetta, Okla.
J. Bedford Shelmire Jr., Dallas, Texas
Jerome F. Sickley, Streator, Ill.
C. Conrad Smith, Augusta, Ga.
Richard E. Strauss, Philadelphia
William Brooks Taylor, Ann Arbor, Mich.
Millard A. Troxell, Cedar Rapids, Iowa
Donald N. Tschan, Wynnewood, Pa.
Robert C. Vanina, Sacramento, Calif.
Silas Wallk, Chicago
Ida Kuritz Walton, Galveston, Texas
Robert G. Walton, Modesto, Calif.
Martin H. Wortzel, Newark, N. J.
Edwin T. Wright, Hollywood, Calif.

ANNOUNCEMENTS

Recent Changes and Clarifications of the Regulations of the American Board of Dermatology and Syphilology, Inc.—It has been suggested that publication in the ARCHIVES of changes in the regulations of the American Board of Dermatology and Syphilology, Inc., would be helpful to many who may not have had recent occasion to refer to the Booklet of Information published by the Board. Accordingly, changes voted at the annual meeting in 1952 and thereafter are given below.

The former "Group A," consisting of candidates who had limited their practice to dermatology and syphilology for 10 or more years, including a period of training satisfactory to the Board, and who were required to take only the oral examination, has been entirely abolished. No new candidates have been accepted in this category since Jan. 1, 1949.

1. In May, 1952, it was voted that any candidate formerly accepted in Group A who had failed to complete the examination successfully would not be eligible for any part of the oral examination until he had first taken and passed the written examination.

The following changes concern reexamination:

2. As the cost of examining a candidate is approximately the same each time, whether the whole or only part of the examination is taken, a reexamination fee of $50 will be charged. After a second failure to complete the examination successfully the candidate must file a new application and pay an additional fee of $75 before he can be reexamined.

3. A candidate who has failed to complete successfully all or part of the examination on two occasions will be required to submit proof of at least six months' additional training in an institution approved for three years of training before he will be eligible for further examination. This additional training may be taken half time over the period of a year, if preferred.

Several changes have been made regarding eligibility for examination:

4. Graduates of medical schools not on the approved list of the Council on Medical Education and Hospitals of the American Medical Association may be eligible on the score of their undergraduate education if they first take and pass the examinations of the National Board of Medical Examiners. The other basic requirements listed in the booklet must still be fulfilled.

A number of candidates have filed application for examination, have been accepted, and then have failed to take the examination. From time to time such candidates years later express their intention to be examined. In some cases they had been accepted on the basis of training no longer considered adequate. It was therefore ruled in 1953 that

5. A candidate once declared eligible for examination shall remain eligible for no more than two succeeding examinations, unless some compelling circumstance, such as military service, shall intervene.

The value of preceptorship training is still the subject of discussion by the Board, and further consideration is to be given. In the meanwhile, the Board in December, 1953, voted to review the entire list of preceptors, a few at a time.

6. In 1952 it was voted that henceforth applicants for the status of preceptor, in addition to the qualifications listed in the Booklet of Information, should be of professorial status in an institution approved for three years of training.

While specific changes in the granting of credit for military service have not been made, it seems well to clarify the Board's stand. Credit toward *training* for such service, unless performed in an approved training institution, is given only under special circumstances, i. e.: when the candidate has already had a significant amount of approved dermatologic training; when his military work is confined to dermatology and syphilology and is closely supervised by a recognized teacher (not merely a specialist certified by the Board), whose qualifications are comparable to those of approved preceptors. Even under these circumstances, credit is not apt to be considerable, as it is felt that in the candidate's interest training should represent a coordinated and consecutive program.

Credit, in part, toward *experience* may be expected for medical military service of more than one year, even though this has not been dermatologic. Credit of any sort is granted only by the Committee on Requirements after consideration of a special Supplementary Application, obtainable on request from the office of the Board. This will not be considered prior to filing the preliminary registration form, as until this has been done the Board has no way of knowing whether the candidate is basically acceptable, and he has no status with the Board. The application should not be submitted until near the end of the tour of duty, as credit will not be awarded for service not yet performed. It must be submitted not later than the application for examination.

Recent editions of the Booklet of Information call attention to the fact that many candidates write, outlining training or experience in related fields of medicine or in military service and asking the Secretary or other members of the Board to inform them how much credit toward training they may expect to receive or how much further training they require at a given point. Individual members of the Board cannot answer such questions. Established provisions are given in the Booklet of Information for the guidance of all. Beyond that, they must be determined by committee action or action of the full Board.

Special credit, when awarded, does not necessarily follow precedent. Credit given in the past has on occasion proved to have been excessive and no favor to the candidate in the long run. On the basis of this experience, the tendency has been to be more conservative, and to recognize the fact that less than three years of straight dermatologic training may well be insufficient.

The 1952 and forthcoming 1954 editions of the Booklet of Information remind candidates that they should not ask for interviews with, or address correspondence to, any member of the Board. This is in accord with the regulations of other specialty boards, the reasons being, in part, that (a) it is an imposition on a man who already devotes a great deal of time to the interests of all candidates; (b) it serves no purpose, as *no individual is empowered to make decisions in the name of the Board.* This cannot be emphasized often or strongly enough.

Information and interpretation of the Board's regulations can be given by the Executive Secretary, whose duty it also is to refer to the appropriate committee all matters requiring action and to report the results. Where these matters fall within the purview of the various officers, they will be so referred.

Another point which always needs stressing is that the responsibility for making contact with the Board, and for ascertaining its rules, rests with the candidate himself. The preliminary registration *must be filed at the beginning of graduate training.*

Certain misconceptions have existed in regard to approval of residency training programs. This approval is accorded jointly by the Board and by the Council on Medical Education and Hospitals of the American Medical Association, and each body acts separately. When a chief of training changes, the institution automatically becomes unapproved until reapplication is made and acted upon. Approval, if given, is retroactive to the date of application. In order to avoid undue disruption and hardship, a candidate is always given credit by the Board for the year in progress when the change occurs, on the basis existing prior thereto. However, credit for succeeding years will depend on the action taken on the new application.

Reconsideration of a training program may be initiated at any time, either by the Council or by the Board. In the case of the latter this may be brought about by various reasons, but especially by the performance of the trainees in examinations, where consistent weaknesses may be revealed, even by those who are passed.

In order to accommodate the large numbers of applicants who sought to enter the field of dermatology after World War II, many institutions were approved for training on a less critical basis. At present, however, the annual registration has leveled off to about 100, and the present list of approved institutions approximates that number, about half being in the three-year group. As it is the Board's avowed purpose to raise progressively the standards of dermatologic training, it is its duty to approve only those institutions which are able to offer the greatest opportunities, and to see that the three-year group in particular represents a consistently high level. Therefore, in 1953 the Board voted to review successively the programs of the entire list of training institutions and to reevaluate these in the light of present standards.

The present membership of the Board is as follows: President, Dr. Nelson Paul Anderson; Vice-President, Dr. George M. Lewis; Secretary-Treasurer, Dr. Anthony C. Cipollaro; Dr. J. Lamar Callaway, Dr. Marcus R. Caro, Dr. Arthur C. Curtis, Dr. Beatrice M. Kesten, Dr. John H. Lamb, and Dr. Francis W. Lynch. The Executive Secretary is Miss Janet Newkirk.

After March 1, 1954, the Board will have an independent office at 129 E. 52d St., New York 22. All files and records, as well as publications, forms, and data will be there, and all communications should be sent to that address.

Prizes Awarded in the Fourth Annual Essay Contest of the American Dermatological Association.—Close competition again marked the Annual Essay Prize Contest sponsored by the American Dermatological Association to stimulate younger investigators to original work in the field of dermatology and syphilology. A total of 11 manuscripts were submitted to the Research Aid Committee of the Association. The high quality of these made it difficult to arrange them in order of merit. In the opinion of the judges, only a few points separated the three outstanding contributions.

The winner of the first prize is Dr. Albert L. Kligman of Philadelphia. His thesis is entitled "The Pathogenesis of Tinea Capitis Due to Microsporon Audouini and Microsporon Canis. II. Histopathologic Findings." Dr. Kligman will receive a cash award of $500 and will present his thesis at the next meeting of the American Dermatological Association, to be held at the Greenbrier Hotel, White Sulphur Springs, W. Va., April 14 to 17, 1954.

Dr. Nichols Nicolaides of Chicago receives a cash award of $300 and second place honorable mention for his paper on "Application of Some Newer Methods of Chemical Analysis to Lipids of the Human Skin Surface." Dr. Peter Flesch and Dr. E. S. Van Scott of Philadelphia receive a cash award of $200 and third place honorable mention for their paper on "Sulfhydryl Groups and Disulfide Linkages in Normal and Pathological Keratinization."

The sponsors of this project are encouraged by the number who participated and they extend heartiest congratulations to the winner. Details of the next contest will be forthcoming soon.

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Archives of Otolaryngology, Sept. 1952: 241-249
The Eye, Ear, Nose & Throat Monthly, April 1950: 200-203
Bulletin of the Johns Hopkins Hospital, Sept. 1948: 225-228
Archives of Otolaryngology, March 1947: 294-297
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References:

1. Ellis, C. C., and others: The Treatment of Psoriasis with Liquor Carbonis Detergens, J. Invest. Dermat. *10*:455, 1948.
2. Sulzberger, M. B., and Wolf, J.: Dermatology, Essentials of Diagnosis and Treatment, Chicago, Year Book Publishers, Inc., 1952, p. 323.

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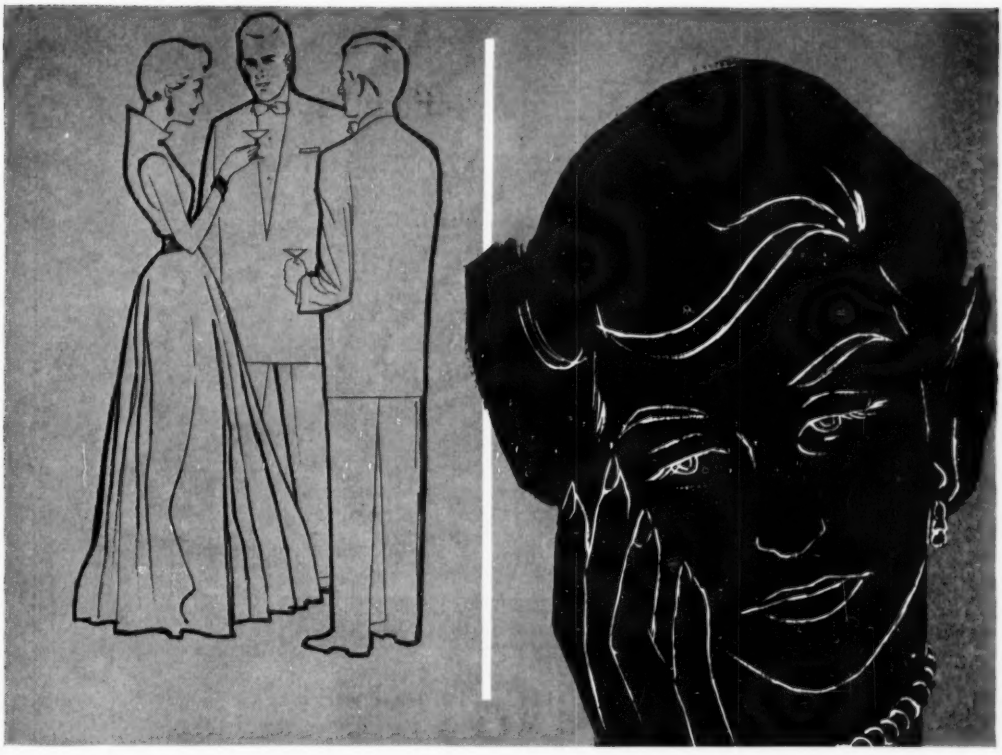

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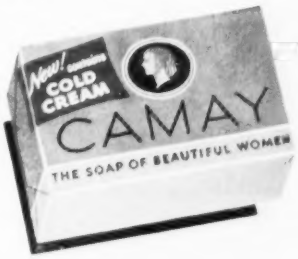

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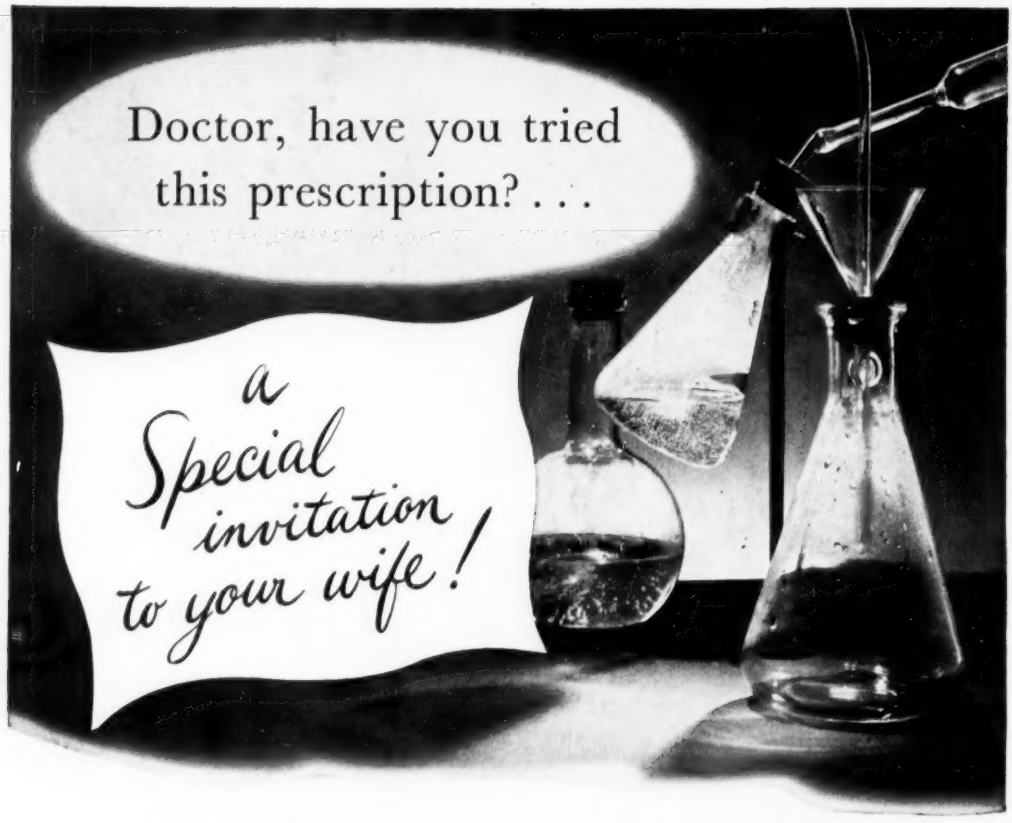

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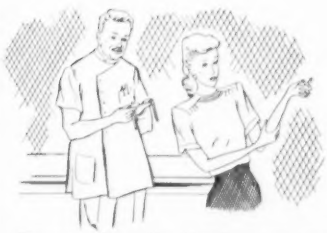

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